

Connecting via Winsock to STN

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LOGINID:SSPTAJRK1626

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page for STN Seminar Schedule - N. America
NEWS 2 AUG 06 CAS REGISTRY enhanced with new experimental property tags
NEWS 3 AUG 06 FSTA enhanced with new thesaurus edition
NEWS 4 AUG 13 CA/Caplus enhanced with additional kind codes for granted
patents
NEWS 5 AUG 20 CA/Caplus enhanced with CAS indexing in pre-1907 records
NEWS 6 AUG 27 Full-text patent databases enhanced with predefined
patent family display formats from INPADOCDB
NEWS 7 AUG 27 USPATOLD now available on STN
CAS REGISTRY enhanced with additional experimental
spectral property data
NEWS 9 SEP 07 STN AnaVist, Version 2.0, now available with Derwent
World Patents Index
NEWS 10 SEP 13 FORIS renamed to SOFIS
NEWS 11 SEP 13 INPADOCDB enhanced with monthly SDI frequency
NEWS 12 SEP 17 CA/Caplus enhanced with printed CA page images from
1967-1998
NEWS 13 SEP 17 Caplus coverage extended to include traditional medicine
patents
NEWS 14 SEP 24 EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15 OCT 02 CA/Caplus enhanced with pre-1907 records from Chemisches
Zentralblatt
NEWS 16 OCT 19 BEILSTEIN updated with new compounds
NEWS 17 NOV 15 Derwent Indian patent publication number format enhanced
NEWS 18 NOV 19 WPIX enhanced with XML display format
NEWS 19 NOV 30 ICSD reloaded with enhancements
NEWS 20 DEC 04 LINPADOCDB now available on STN
NEWS 21 DEC 14 BEILSTEIN pricing structure to change
NEWS 22 DEC 17 USPATOLD added to additional database clusters
NEWS 23 DEC 17 IMSDRUGCONF removed from database clusters and STN
NEWS 24 DEC 17 DGENE now includes more than 10 million sequences
NEWS 25 DEC 17 TOXCENTER enhanced with 2008 MeSH vocabulary in
MEDLINE segment
NEWS 26 DEC 17 MEDLINE and LMEADLINE updated with 2008 MeSH vocabulary
NEWS 27 DEC 17 CA/Caplus enhanced with new custom IPC display formats
NEWS 28 DEC 17 STN Viewer enhanced with full-text patent content
from USPATOLD
NEWS 29 JAN 02 STN pricing information for 2008 now available
NEWS 30 JAN 16 CAS patent coverage enhanced to include exemplified
prophetic substances
NEWS 31 JAN 28 USPATFULL, USPAT2, and USPATOLD enhanced with new

				custom IPC display formats
NEWS 32	JAN 28			MARPAT searching enhanced
NEWS 33	JAN 28			USGENE now provides USPTO sequence data within 3 days of publication
NEWS 34	JAN 28			TOXCENTER enhanced with reloaded MEDLINE segment
NEWS 35	JAN 28			MEDLINE and LMEDLINE reloaded with enhancements
NEWS EXPRESS	19 SEPTEMBER 2007:			CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER VERSION IS DATED 19 SEPTEMBER 2007.
NEWS HOURS				STN Operating Hours Plus Help Desk Availability
NEWS LOGIN				Welcome Banner and News Items
NEWS IPC8				For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 15:49:32 ON 05 FEB 2008

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=> file reg
COST IN U.S. DOLLARS          SINCE FILE          TOTAL
                               ENTRY          SESSION
FULL ESTIMATED COST          1.26          1.26
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FILE 'REGISTRY' ENTERED AT 15:52:55 ON 05 FEB 2008
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

```
STRUCTURE FILE UPDATES:      4 FEB 2008   HIGHEST RN 1001463-85-9
DICTIONARY FILE UPDATES:    4 FEB 2008   HIGHEST RN 1001463-85-9
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New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

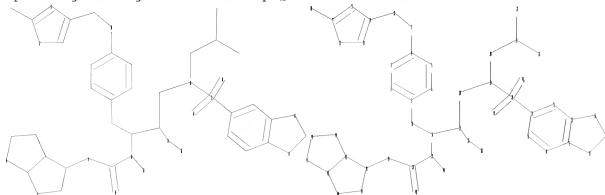
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10560500\Struc 1.str



chain nodes :

7 8 14 15 16 17 18 19 20 21 22 23 24 26 27 28 29 46 47 48 49

50

ring nodes :

1 2 3 4 5 6 9 10 11 12 13 25 30 31 32 33 34 35 36 37 38 39 40

41 42 43 44 45

chain bonds :

1-15 4-7 7-8 8-9 12-14 15-16 16-17 16-27 17-18 17-26 18-19 19-20 19-24

20-21 21-22 21-23 24-25 24-46 24-47 26-50 27-28 27-49 28-29 28-48 29-30

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 9-10 9-13 10-11 11-12 12-13 25-31 25-35 30-39

30-42 31-32 32-33 32-36 33-34 33-38 34-35 36-37 37-38 39-40 40-41 41-42

41-43 42-45 43-44 44-45

exact/norm bonds :

4-7 7-8 9-10 9-13 10-11 11-12 12-13 16-27 17-26 18-19 19-20 19-24 24-25

24-46 24-47 27-28 28-29 28-48 29-30 30-39 30-42 32-36 33-38 36-37 37-38

39-40 40-41 41-42 41-43 42-45 43-44 44-45

exact bonds :

1-15 8-9 12-14 15-16 16-17 17-18 20-21 21-22 21-23 26-50 27-49

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 25-31 25-35 31-32 32-33 33-34 34-35

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:Atom 10:Atom

11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:Atom 26:CLASS

27:CLASS 28:CLASS 29:CLASS 30:Atom 31:Atom 32:Atom 33:Atom 34:Atom 35:Atom

36:Atom 37:Atom 38:Atom 39:Atom 40:Atom 41:Atom 42:Atom 43:Atom 44:Atom

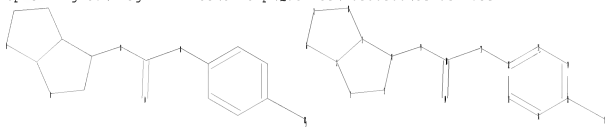
45:Atom 46:CLASS 47:CLASS 48:CLASS 49:CLASS 50:CLASS

10560500.trn

L1 STRUCTURE UPLOADED

=>

Uploading C:\Program Files\Stnexp\Queries\10560500\Struc 2.str



```
chain nodes :
9 10 11 18 19
ring nodes :
1 2 3 4 5 6 7 8 12 13 14 15 16 17
chain bonds :
4-9 9-10 10-11 10-19 11-12 15-18
ring bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 6-7 7-8 12-13 12-17 13-14 14-15 15-16
16-17
exact/norm bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 4-9 6-7 7-8 9-10 10-11 10-19 11-12
exact bonds :
15-18
normalized bonds :
12-13 12-17 13-14 14-15 15-16 16-17
```

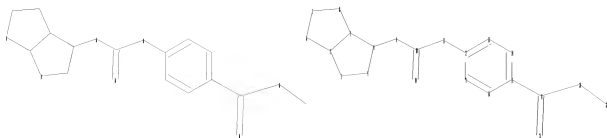
Match level :

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1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
```

L2 STRUCTURE UPLOADED

=>

Uploading C:\Program Files\Stnexp\Queries\10560500\Struc 3.str



```

chain nodes :
9 10 11 18 19 20 21 22
ring nodes :
1 2 3 4 5 6 7 8 12 13 14 15 16 17
chain bonds :
4-9 9-10 10-11 10-19 11-12 15-18 18-20 18-21 20-22
ring bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 6-7 7-8 12-13 12-17 13-14 14-15 15-16
16-17
exact/norm bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 4-9 6-7 7-8 9-10 10-11 10-19 11-12 18-20
18-21 20-22
exact bonds :
15-18
normalized bonds :
12-13 12-17 13-14 14-15 15-16 16-17

```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS

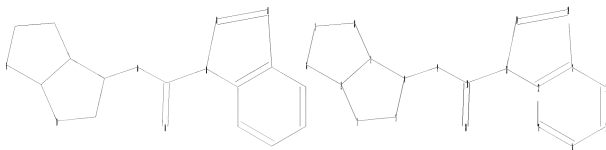
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L3 STRUCTURE UPLOADED

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=>
Uploading C:\Program Files\Stnexp\Queries\10560500\Struc 4.str

```



```

chain nodes :
9 10 18
ring nodes :
1 2 3 4 5 6 7 8 11 12 13 14 15 16 17 19 20
chain bonds :
4-9 9-10 10-11 10-18
ring bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 6-7 7-8 11-12 11-19 12-13 12-17 13-14
13-20 14-15 15-16 16-17 19-20
exact/norm bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 4-9 6-7 7-8 9-10 10-11 10-18 11-12 11-19
13-20 19-20
normalized bonds :
12-13 12-17 13-14 14-15 15-16 16-17

```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
11:CLASS 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:Atom
20:Atom

```

L4 STRUCTURE UPLOADED

=> l1 exa

SAMPLE SEARCH INITIATED 15:53:51 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 0 TO 0
PROJECTED ANSWERS: 0 TO 0

L5 0 SEA EXA SAM L1

=> l1 exa full

FULL SEARCH INITIATED 15:53:56 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 20 TO ITERATE

10560500.trn

100.0% PROCESSED 20 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L6 2 SEA EXA FUL L1

=> 12 exa full
FULL SEARCH INITIATED 15:54:02 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

L7 8 SEA EXA FUL L2

=> 13 exa full
FULL SEARCH INITIATED 15:54:08 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

L8 1 SEA EXA FUL L3

=> 14 exa ful
FULL SEARCH INITIATED 15:54:14 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

L9 1 SEA EXA FUL L4

=> file hcaplus		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	240.32	241.58

FILE 'HCAPLUS' ENTERED AT 15:54:19 ON 05 FEB 2008
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FILE COVERS 1907 - 5 Feb 2008 VOL 148 ISS 6
FILE LAST UPDATED: 4 Feb 2008 (20080204/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> 16 and 17

```

      34 L6
      24 L7
L10   1 L6 AND L7

```

=> 16 and 18

```

      34 L6
      1 L8
L11   1 L6 AND L8

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=> 16 and 19

```

      34 L6
      1 L9
L12   1 L6 AND L9

```

=> 110 and 111 and 112

```

L13   1 L10 AND L11 AND L12

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=> d ibib abs hitstr

L13 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:14172 HCAPLUS

DOCUMENT NUMBER: 142:114047

TITLE: A preparation of furofuranyl derivative, useful as inhibitor of HIV aspartyl protease

INVENTOR(S): Roberts, John Charles; Toczko, Jennifer Fell

PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; Martin, Michael Tolar

SOURCE: PCI Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000249	A2	20050106	WO 2004-US20353	20040625
WO 2005000249	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1638960	A2	20060329	EP 2004-777060	20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007521277	T	20070802	JP 2006-517643	20040625
US 2006148865	A1	20060706	US 2005-560500	20051212
PRIORITY APPLN. INFO.:			US 2003-483002P	P 20030627
			WO 2004-US20353	W 20040625
OTHER SOURCE(S):		CASREACT 142:114047		
GI				

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

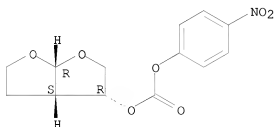
AB The invention relates to a preparation of furofuranyl derivative I, useful as inhibitor of HIV aspartyl protease (no biol. data). For instance, I was prepared via deprotection of II and coupling with III with a yield of 90% (example 2).

IT 192/25-55-6P 820250-08-6P 820250-09-7P
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)

RN 192/25-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

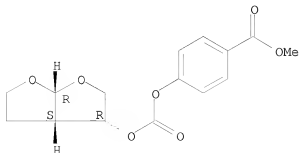
Absolute stereochemistry. Rotation (-).



RN 820250-08-6 HCAPLUS

CN Benzoic acid, 4-[[[(3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl]oxy]carbonyl]oxy]-, methyl ester (CA INDEX NAME)

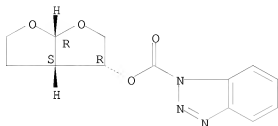
Absolute stereochemistry.



RN 820250-09-7 HCAPLUS

CN 1H-Benzotriazole-1-carboxylic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



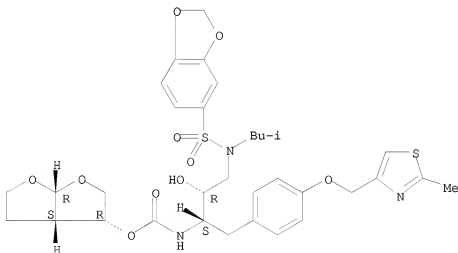
IT 313682-08-5P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



=> log h

COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE

ENTRY

10.83

TOTAL

SESSION

252.41

10560500.trn

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-0.80	-0.80

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:55:14 ON 05 FEB 2008

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAJRK1626

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
SESSION RESUMED IN FILE 'HCAPLUS' AT 15:59:52 ON 05 FEB 2008
FILE 'HCAPLUS' ENTERED AT 15:59:52 ON 05 FEB 2008
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	10.83	252.41

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-0.80	-0.80

=> 16
L14 34 L6

=> 17
L15 24 L7

=> d ibib abs hitstr 1-34

L15 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1275513 HCAPLUS
DOCUMENT NUMBER: 147:502340
TITLE: Process for preparation of carbamic acid bisfuranyl
esters as HIV protease inhibitors and their use in the
treatment of retroviral infection
INVENTOR(S): Crawford, Kenneth R.; Dowdy, Eric D.; Gutierrez,
Arnold; Polniaszek, Richard P.; Yu, Richard Hung Chiu
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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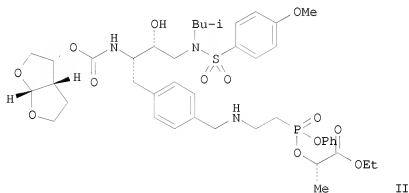
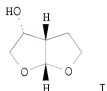
WO 2007126812 A2 20071108 WO 2007-US7564 20070329
 WO 2007126812 A3 20071221
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 2008004242 A1 20080103 US 2007-729522 20070329

PRIORITY APPLN. INFO.: US 2006-787126P P 20060329

OTHER SOURCE(S): CASREACT 147:502340

GI



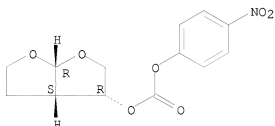
AB A process for the synthesis of bisfuran intermediates, e.g., I useful for preparing antiviral HIV protease inhibitor compds. is hereby disclosed. Example compound II was prepared as adipic acid salt and succinic acid salts, using intermediate I as the key component in the preparation. The invention compds. were evaluated for their HIV protease inhibitory activity (no data).

IT 192725-55-6P

RL: BSU (Biological study, unclassified); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of carbamic acid bisfuran ester compds. as HIV protease inhibitors useful in treatment and prevention of retroviral infection)

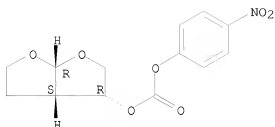
RN 192725-55-6 HCAPLUS
 CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:1131417 HCAPLUS
 DOCUMENT NUMBER: 148:33642
 TITLE: Research and Development of an Efficient Synthesis of Hexahydrofuro[2,3-b]furan-3-ol Moiety-A Key Component of the HIV Protease Inhibitor Candidates
 AUTHOR(S): Yu, Richard H.; Poiniaszek, Richard P.; Becker, Mark W.; Cook, Charles M.; Yu, Lok Him L.
 CORPORATE SOURCE: Process Research Department, Gilead Sciences, Inc., Foster City, CA, 94404, USA
 SOURCE: Organic Process Research & Development (2007), 11(6), 972-980
 CODEN: OPRDFK; ISSN: 1083-6160
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 148:33642
 AB A highly efficient method for the synthesis of racemic hexahydrofuro[2,3-b]furan-3-ol has been developed utilizing a lanthanide catalyst, such as Yb(fod)₃, to promote condensation of 2,3-dihydrofuran and glycolaldehyde dimer. Access to either optically enriched enantiomer of bisfuran alc. can be obtained by using this method employing chiral ligands with the lanthanide catalyst. This method has been demonstrated to be a robust and scalable process with potential application for the construction of a variety of furo[2,3-b]furan derivs.
 IT 192725-55-6P
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
 (scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)
 RN 192725-55-6 HCAPLUS
 CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:449362 HCAPLUS

DOCUMENT NUMBER: 145:8179

TITLE: Process for the preparation of pyrimidinyl aminodiphenylhexane derivatives as retroviral protease inhibiting prodrugs

INVENTOR(S): Kumar, Gondi N.; Herrin, Thomas R.; Kempf, Dale J.; Betebenner, David A.; Chen, Xiaoqi; Norbeck, Daniel W.; Sham, Hing Leung; Patel, Ketan M.; Liu, Jih-Hua; Tien, Jieh-Heh J.; Stoner, Eric J.; Stengel, Peter J.; Plata, Daniel J.; Oliver, Patricia A.; Kolaczowski, Lawrence; Hannick, Steven M.; Dickman, Daniel A.; Cooper, Arthur J.; Condon, Stephen L.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: Aust. Pat. Appl., 252 pp.

CODEN: AUXXCM

DOCUMENT TYPE: Patent

LANGUAGE: English

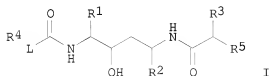
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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AU 2004201149	A1	20040422	AU 2004-201149	20040318
AU 2004201149	B2	20070802		
AU 2007231810	A1	20071129	AU 2007-231810	20071101
PRIORITY APPLN. INFO.:			AU 2001-13690	A3 20010112
			AU 2004-201149	A3 20040318

OTHER SOURCE(S): MARPAT 145:8179

GI



AB Pyrimidinyl aminodiphenylhexane derivs. I, wherein R1 and R2 are independently lower alkyl, cycloalkyl-alkyl, aryl-alkyl; R3 is lower

alkyl, cycloalkyl-alkyl, hydroxy-alkyl; R4 is aryl, heterocyclic; R5 is five- or six-membered heterocycle containing at least one nitrogen atom; L is O, S, NH, N-alkyl, , N-cycloalkyl, N-cycloalkyl-alkyl, O-alkylenyl, SO-alkylenyl, S(O)2-alkylenyl, alkylenyl-O, alkylenyl-S, alkylenyl, alkenylenyl, were prepared and tested in vitro and in human as retroviral protease inhibiting prodrugs. Thus, (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-[2S-(1-tetrahydropyrimid-2-onyl)-3-methylbutanoyl]amino-1,6-diphenylhexane was prepared via coupling of (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-amino-1,6-diphenylhexane with 2S-(1-tetrahydro-pyrimid-2-onyl)-3-methylbutanoic acid. The present invention relates to novel compds. and a composition and method for inhibiting retroviral proteases and in particular for inhibiting human immunodeficiency virus (HIV) protease, a composition and method for inhibiting a retroviral infection and in particular an HIV infection, processes for making the compds. and synthetic intermediates employed in the processes. While the compound of the invention can be administered as the sole active pharmaceutical agent, it can also be used in combination with one or more immunomodulators, antiviral agents, other antiinfective agents, or vaccines. The compds. of the invention are useful for inhibiting retroviral protease, in particular HIV protease, in vitro or in vivo (especially in mammals and in particular in humans). Total daily dose administered to a human or other mammal host in single or divided doses may be in amts., for example, from 0.001 to 300 mg/kg body weight daily and more usually 0.1 to 20 mg/kg body weight daily.

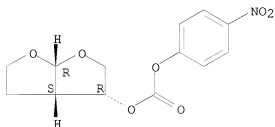
IT 192725-55-6P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of pyrimidinyl aminodiphenylhexane derivs. as retroviral protease inhibiting prodrugs)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1154569 HCAPLUS

DOCUMENT NUMBER: 143:406046

TITLE: Preparation of azacyclosteroids as histamine-3 receptor ligands

PATENT ASSIGNEE(S): Abbott Laboratories, USA; Zhao, Chen; Sun, Minghua; Cowart, Marlon D.; Bennani, Youssef L.

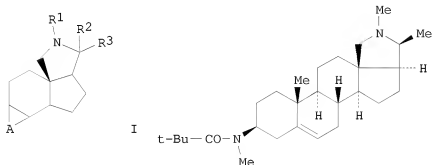
SOURCE: PCT Int. Appl., 185 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005100377	A1	20051027	WO 2005-US14019	20050406
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005245495	A1	20051103	US 2004-819849	20040407
CA 2562189	A1	20051027	CA 2005-2562189	20050406
EP 1735332	A1	20061227	EP 2005-738987	20050406
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2007532583	T	20071115	JP 2007-507579	20050406
MX 2006PA11669	A	20070123	MX 2006-PA11669	20061006
PRIORITY APPLN. INFO.:			US 2004-819849	A 20040407
			WO 2005-US14019	W 20050406
OTHER SOURCE(S):			CASREACT 143:406046; MARPAT 143:406046	
GI				

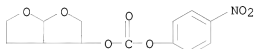


AB Azacyclosteroids of formula I [R1 = H, acetyl, alkyl, fluoroalkyl, cycloalkyl; R2, R3 = H, alkyl; R2R3 = 3-6 membered ring; A = (substituted) benzo or naphthyl fused ring] are prepared as histamine H3 receptor ligands. Thus, II was prepared starting from conessine. Representative compds. had binding affinities between 810 nM to 0.12 nM.

IT 854745-99-6

RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of azacyclosteroids as histamine H3 receptor ligands)

RN 854745-99-6 HCAPLUS
 CN Carbonic acid, hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1154157 HCAPLUS

DOCUMENT NUMBER: 143:422465

TITLE: Preparation of phosphonate analogs of HIV protease inhibitors and methods for identifying anti-HIV therapeutic compounds

INVENTOR(S): Arimilli, Murty N.; Becker, Mark M.; Birkus, Gabriel

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 1034 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

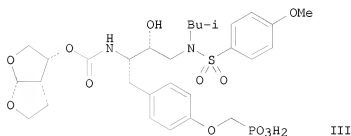
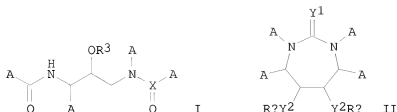
FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005239054	A1	20051027	US 2003-740694	20031222
WO 2003090690	A2	20031106	WO 2003-US12901	20030425
WO 2003090690	A3	20040624		
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WO 2003091264	A2	20031106	WO 2003-US12926	20030425
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WO 2003090691 A3 20060209
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 US 2004121316 A1 20040624 US 2003-424186 20030425
 US 2005197320 A1 20050908 US 2003-424130 20030425
 US 2005209197 A1 20050922 US 2003-423496 20030425
 CN 101041669 A 20070926 CN 2006-10154203 20030425
 CN 101074242 A 20071121 CN 2007-10085746 20030425
 ZA 2004009376 A 20050914 ZA 2004-9376 20041122
 ZA 2004009377 A 20060329 ZA 2004-9377 20041122
 AU 2004309379 A1 20050714 AU 2004-309379 20041222
 CA 2550730 A1 20050714 CA 2004-2550730 20041222
 WO 2005064008 A1 20050714 WO 2004-US42991 20041222
 WO 2005064008 A9 20060928
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 EP 1711617 A1 20061018 EP 2004-817046 20041222
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 JP 2007515184 T 20070614 JP 2006-547281 20041222
 PRIORITY APPLN. INFO.:
 US 2002-375622P P 20020426
 US 2002-375665P P 20020426
 US 2002-375779P P 20020426
 US 2002-375834P P 20020426
 US 2003-423496 A2 20030425
 US 2003-424130 A2 20030425
 US 2003-424186 A2 20030425
 US 2003-465721P P 20030425
 US 2003-465810P P 20030425
 US 2003-465824P P 20030425
 WO 2003-US12901 A2 20030425
 WO 2003-US312926 A2 20030425
 WO 2003-US312943 A2 20030425
 CN 2003-812478 A3 20030425
 CN 2003-814963 A3 20030425
 US 2003-740694 A 20031222
 WO 2004-US42991 W 20041222

GI



AB The invention relates to phosphonate-substituted carbamates I and cyclic ureas II [wherein A = A1, A2, or W3 with the proviso that at least one of A = A1; A1 = [Y2(CR2R2)1-12]0-12Y2W6; A2 = [Y2(CR2R2)1-12]0-12Y2W3; W3 = substituted (hetero)cyclyl; R5, C(Y1)R5, C(Y1)W5, SO2R5, or SO2W5; W5 = substituted (hetero)cyclyl; W6 = triphosphono-substituted W3; Y1 = O, S, N(Rx), N(O)(Rx), N(ORx), or N(N(Rx)2); Y2 = independently a bond, O, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), N(N(Rx)2), SO0-2, or SO0-2SO0-2; Rx = independently H, R1, W3, a protecting group, etc.; R1 = independently H or alkyl; R2 = independently H, R1, halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SO-2Rx, substituted alkyl, alkenyl, alkynyl, etc.; R3 = halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SRx, SORx, SO2Rx, OC(Y1)Rx, OC(Y1)ORx, C(Y1)Rx, etc. with provisos; R5 = substituted alkyl, alkenyl, or alkynyl; or pharmaceutically acceptable salts, hydrates, and formulations thereof] and other phosphonate-substituted analogs of HIV protease inhibitors for treating AIDS and other antiviral infections, as well as for use in assays for the detection of HIV protease. Comps. of the invention inhibit reverse transcriptase activity and have improved intracellular half-life compared to analogs not having the phosphonate or phosphonate prodrug. Libraries of such comps. were screened optionally using the novel enzyme GS-7340 ester hydrolase. Comps. and methods relating to GS-7340 ester hydrolase also are provided. Examples include preps. for non-nucleoside phosphonate protease inhibitors. In addition, extensive biol. data regarding PBMC uptake and metabolism, serum stability, and alkaline phosphatase protease inhibitor (ALPPI) activity of selected phosphonate-substituted prodrugs is presented. For instance, a 9-step reaction sequence starting from N-tert-butoxycarbonyl-O-benzyl-L-tyrosine provided III (K_i ≤10 pM for ALPPI activity). The synthesis involved multiple protection and deprotection steps along with coupling reactions using isobutylamine, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-2-yl 4-nitrophenyl carbonate, and dibenzyl hydroxymethylphosphonate.

IT 192725-55-6P

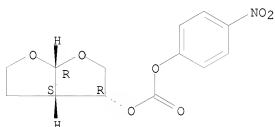
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of phosphonate-substituted HIV protease inhibitors for treatment of AIDS and other viral infections)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:1106795 HCAPLUS

DOCUMENT NUMBER: 143:367448

TITLE: Preparation of azacyclosteroid histamine-3 receptor ligands

INVENTOR(S): Zhao, Chen; Sun, Minghua; Cowart, Marlon D.; Bennani, Youssef L.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 85 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

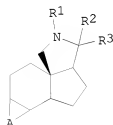
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

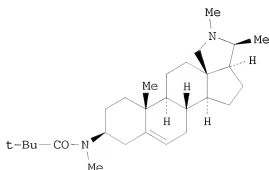
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005227953	A1	20051013	US 2005-96382	20050401
PRIORITY APPLN. INFO.:			US 2004-560151P	P 20040407
OTHER SOURCE(S):	MARPAT	143:367448		

GI



I



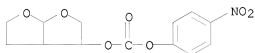
II

AB Azacyclosteroids of formula I [R1 = H, acetyl, alkyl, fluoroalkyl, cycloalkyl; R2, R3 = H, alkyl; R2R3 = 3-6-membered ring; A = fused (substituted) naphthyl or benzo ring] are prepared as histamine H2 receptor ligands. Thus, II was prepared starting from conessine. The compds. had binding affinities from about 810 nM to 0.12 nM against histamine-3 receptor.

IT 854745-99-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of azacyclosteroids as histamine H3 receptor ligands)

RN 854745-99-6 HCAPLUS

CN Carbonic acid, hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)



L15 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:612479 HCAPLUS

DOCUMENT NUMBER: 143:97530

TITLE: Preparation of phosphonate analogs of HIV protease inhibitors and methods for identifying anti-HIV therapeutic compounds

INVENTOR(S): Arimilli, Murty N.; Becker, Mark M.; Birkus, Gabriel; Bryant, Clifford; Chen, James M.; Chen, Xiaowu; Cihlar, Tomas; Dastgah, Azar; Eisenberg, Eugene J.; Fardis, Maria; Hatada, Marcos; He, Gong-Xin; Jin, Haolun; Kim, Choung U.; Lee, William A.; Lee, Christopher P.; Lin, Kuei-Ying; Liu, Hongtao; Mackman, Richard L.; McDermott, Martin J.; Mitchell, Michael L.; Nelson, Peter H.; Pyun, Hyung-Jung; Rowe, Tanisha D.; Sparacino, Mark; Swaminathan, Sundaramoorthi; Tario, James D.; Wang, Jianying; Williams, Matthew A.; Xu, Lianhong; Yang, Zheng-Yu; Yu, Richard H.; Zhang, Jiancun; Zhang, Lijun

PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA

SOURCE: PCT Int. Appl., 1723 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 9

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005064008	A1	20050714	WO 2004-US42991	20041222
WO 2005064008	A9	20060928		

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TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
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 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG

US 2005239054 A1 20051027 US 2003-740694 20031222
 AU 2004309379 A1 20050714 AU 2004-309379 20041222
 CA 2550730 A1 20050714 CA 2004-2550730 20041222
 EP 1711617 A1 20061018 EP 2004-817046 20041222

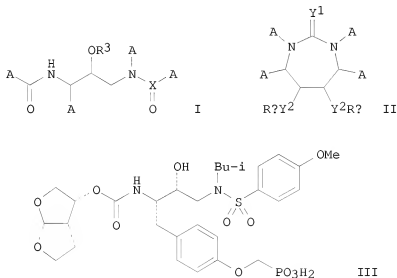
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JP 2007515184 T 20070614 JP 2006-547281 20041222

PRIORITY APPLN. INFO.:

US 2003-740694 A 20031222
 US 2002-375622P P 20020426
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 US 2002-375779P P 20020426
 US 2002-375834P P 20020426
 US 2003-423496 A2 20030425
 US 2003-424130 A2 20030425
 US 2003-424186 A2 20030425
 US 2003-465721P P 20030425
 US 2003-465810P P 20030425
 US 2003-465824P P 20030425
 WO 2003-US12901 A2 20030425
 WO 2003-US12926 A2 20030425
 WO 2003-US12943 A2 20030425
 WO 2004-US42991 W 20041222

GI



AB The invention relates to phosphonate-substituted carbamates I and cyclic ureas II [wherein A = A1, A2, or W3 with the proviso that at least one of

A = Al; A1 = [Y2(CR2R2)1-12]0-12Y2W6; A2 = [Y2(CR2R2)1-12]0-12Y2W3; W3 = substituted (hetero)cyclyl, R5, C(Y1)R5, C(Y1)W5, SO2R5, or SO2W5; W5 = substituted (hetero)cyclyl; W6 = triphosphono-substituted W3; Y1 = O, S, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), or N(N(Rx)2); Y2 = independently a bond, O, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), N(N(Rx)2), SOO-2, or SOO-2SOO-2; Rx = independently H, R1, W3, a protecting group, etc.; R1 = independently H or alkyl; R2 = independently H, R1, halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SO-2Rx, substituted alkyl, alkenyl, alkynyl, etc.; R3 = halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SRx, SORx, SO2Rx, OC(Y1)Rx, OC(Y1)ORx, C(Y1)Rx, etc. with provisos; R5 = substituted alkyl, alkenyl, or alkynyl; or pharmaceutically acceptable salts, hydrates, and formulations thereof] and other phosphonate-substituted analogs of HIV protease inhibitors for treating AIDS and other antiviral infections, as well as for use in assays for the detection of HIV protease. Compds. of the invention inhibit reverse transcriptase activity and have improved intracellular half-life compared to analogs not having the phosphonate or phosphonate prodrug. Libraries of such compds. were screened optionally using the novel enzyme GS-7340 ester hydrolase. Compns. and methods relating to GS-7340 ester hydrolase also are provided. Examples include preps. for non-nucleoside phosphonate protease inhibitors. In addition, extensive biol. data regarding PBMC uptake and metabolism, serum stability, and alkaline phosphatase protease inhibitor (ALPPI) activity of selected phosphonate-substituted prodrugs is presented. For instance, a 9-step reaction sequence starting from N-tert-butoxycarbonyl-O-benzyl-L-tyrosine provided III (Ki ≤10 pM for ALPPI activity). The synthesis involved multiple protection and deprotection steps along with coupling reactions using isobutylamine, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-2-yl 4-nitrophenyl carbonate, and dibenzyl hydroxymethylphosphonate.

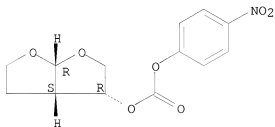
IT 192725-55-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phosphonate-substituted HIV protease inhibitors for treatment of AIDS and other viral infections)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:589363 HCAPLUS

DOCUMENT NUMBER: 143:248118

TITLE: Synthesis and antiviral activities of novel

AUTHOR(S): N-alkoxy-arylsulfonamide-based HIV protease inhibitors
Sherrill, Ronald G.; Furfine, Eric S.; Hazen, Richard
J.; Miller, John F.; Reynolds, David J.; Sammond,
Douglas M.; Spaltenstein, Andrew; Wheelan, Pat;
Wright, Lois L.

CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709,
USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2005),
15(15), 3560-3564
CODEN: BMCLE8; ISSN: 0960-894X

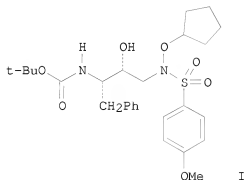
PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:248118

GI



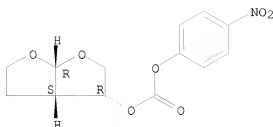
AB A series of N-alkoxy-arylsulfonamide HIV protease inhibitors, e.g., I,
with low picomolar enzyme activity and single digit nanomolar antiviral
activity is disclosed.

IT 192725-55-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, antiviral activity, HIV protease inhibitory activity, and
structure-activity relationship of N-alkoxy arylsulfonamide derivs.
starting from alkoxyamines, phenylalanine-epoxide, and arylsulfonyl
chlorides)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl
ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:589326 HCAPLUS

DOCUMENT NUMBER: 143:267225

TITLE: Novel P1 chain-extended HIV protease inhibitors possessing potent anti-HIV activity and remarkable inverse antiviral resistance profiles

AUTHOR(S): Miller, John F.; Brieger, Michael; Furfine, Eric S.; Hazen, Richard J.; Kaldor, Istvan; Reynolds, David; Sherrill, Ronald G.; Spaltenstein, Andrew

CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(15), 3496-3500

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:267225

AB A novel series of tyrosine-derived HIV protease inhibitors was synthesized and evaluated for in vitro antiviral activity against wild-type virus and two protease inhibitor-resistant viruses. All of the compds. had wild-type antiviral activities that were similar to or greater than several currently marketed HIV protease inhibitors. In addition, a number of compds. in this series were more potent against the drug-resistant mutant viruses than they were against wild-type virus.

IT 192725-55-6P

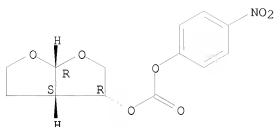
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of P1 chain-extended HIV protease inhibitors possessing potent anti-HIV activity and remarkable inverse antiviral resistance profiles)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:588404 HCAPLUS

DOCUMENT NUMBER: 143:133693

TITLE: Preparation of amino acid derivatives as HIV protease inhibitors

INVENTOR(S): Degoe, David A.; Flentge, Charles A.; Flosi, William J.; Grampovnik, David J.; Kempf, Dale J.; Klein, Larry L.; Yeung, Ming C.; Randolph, John T.; Wang, Xiu C.; Yu, Su

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 279 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005148623	A1	20050707	US 2004-8713	20041209
PRIORITY APPLN. INFO.:			US 2003-528974P	P 20031211

OTHER SOURCE(S): MARPAT 143:133693

AB The invention relates to amino acid derivs. A-NHCHR6CHR5CHR4CHR3NHCOCHR2NHCO2R1 [A is an amino acid or acyl residue of defined structure; R1, R2, R3, R6 are independently (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl or heteroaryl; R4, R5 are H (not both), OH or substituted hydroxyl], including pharmaceutically-acceptable salts, prodrugs or stereoisomers, having HIV protease inhibitory activity. Thus, Me (1S,4R,6S,7S,10S)-7-benzyl-1,10-di-tert-butyl-6-hydroxy-2,9,12-trioxo-4-[4-(2-pyridinyl)benzyl]-13-oxa-3,8,11-triazatetradec-1-ylcarbamate was prepared by a multistep procedure, which includes the reaction of intermediate tert-Bu (1S,2S,4R)-4-amino-1-benzyl-2-hydroxy-5-[4-(2-pyridinyl)phenyl]pentylcarbamate with N-protected L-tert-leucine. Compds. of the invention showed EC50 values in the range 0.7 nM to >3.2 μM against wild-type HIV.

IT 192725-55-6P

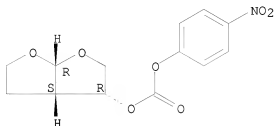
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino acid derivs. as HIV protease inhibitors)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:527407 HCAPLUS

DOCUMENT NUMBER: 143:59982

TITLE: Preparation of HIV protease inhibitors, in particular imidazolidine derivatives

INVENTOR(S): Flentge, Charles A.; Chen, Hui-Ju; DeGoey, David A.; Flosi, William J.; Grampovnik, David J.; Huang, Peggy P.; Kempf, Dale J.; Klein, Larry L.; Krueger, Allan C.; Madigan, Darold L.; Randolph, John T.; Sun, Minghua; Yeung, Ming C.; Zhao, Chen

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 287 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005131042	A1	20050616	US 2003-733915	20031211
CA 2549389	A1	20050707	CA 2004-2549389	20041110
WO 2005061450	A2	20050707	WO 2004-US37745	20041110
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW</p> <p>RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG</p>				
EP 1709037	A2	20061011	EP 2004-810802	20041110
<p>R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS</p>				
JP 2007513944	T	20070531	JP 2006-543826	20041110
MX 2006PA06610	A	20060831	MX 2006-PA6610	20060609
PRIORITY APPLN. INFO.:			US 2003-733915	A 20031211

WO 2004-US37745 W 20041110

OTHER SOURCE(S): MARPAT 143:59982
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

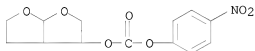
AB Title compds. of formula ANH(CHR)(CHR1)(CHR2)NR3S(O2)R4 (I) [wherein A = alkylcarbonyl, arylsulfonyl, 1,3-substituted 2-oxoimidazolidinyl, 2,4-dioxoimidazolidinyl, etc.; X, Y = independently O, S, NH; R = (un)substituted alk(en)yl, cycloalk(en)yl, hetero/arylalkyl, etc.; R1 = OH and derivs., OPO3H and derivs., OSO2H and derivs., etc.; R2 = H; R3 = halo/alkyl, halo/alkenyl, (un)substituted cycloalk(en)yl, aryl; R4 = (un)substituted cycloalk(en)yl, heterocyclyl, hetero/aryl] were prepared as HIV protease inhibitors. For example, II was prepared, in 62% yield, by coupling acid III (preparation given) with amine IV (preparation given). I

showed
antiviral activity against Wild-Type HIV with EC50 in the range of 1 nM to 100 nM.

IT 854745-99-6P, Hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl carbonate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of HIV protease inhibitors, in particular imidazolidine derivs.)

RN 854745-99-6 HCAPLUS

CN Carbonic acid, hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)



L15 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2008 ACS on SIN

ACCESSION NUMBER: 2005:527398 HCAPLUS

DOCUMENT NUMBER: 143:78485

TITLE: Preparation of amino acid derivatives as HIV protease inhibitors

INVENTOR(S): Degeoey, David A.; Flentge, Charles A.; Flosi, William J.; Grampovnik, David J.; Kempf, Dale J.; Klein, Larry L.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 204 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

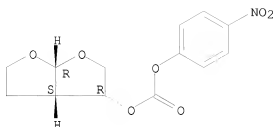
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2005131017 A1 20050616 US 2003-733946 20031211
 CA 2549098 A1 20050630 CA 2004-2549098 20041209
 WO 2005058841 A2 20050630 WO 2004-US41658 20041209
 WO 2005058841 A3 20060309
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI,
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
 MR, NE, SN, TD, TG
 EP 1697344 A2 20060906 EP 2004-813910 20041209
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK,
 BA, HR, IS, YU
 JP 2007516260 T 20070621 JP 2006-544070 20041209
 MX 2006PA06612 A 20060831 MX 2006-PA6612 20060609
 PRIORITY APPLN. INFO.: US 2003-733946 A 20031211
 WO 2004-US41658 W 20041209
 OTHER SOURCE(S): CASREACT 143:78485; MARPAT 143:78485
 AB The invention relates to amino acid derivs. A-
 NHCHR6CHR5CHR4CHR3NHCOCHR2NHCO2R1 [A is an amino acid or acyl residue of
 defined structure; R1, R2, R3, R6 are independently (un)substituted alkyl,
 alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl or
 heteroaryl; R4, R5 are H (not both), OH or substituted hydroxyl],
 including pharmaceutically-acceptable salts, stereoisomers, esters or
 prodrugs, having HIV protease inhibitory activity. Thus, Me
 (1S,4R,6S,7S,10S)-7-benzyl-1,10-di-tert-butyl-6-hydroxy-2,9,12-trioxo-4-[4-
 (2-pyridinyl)benzyl]-13-oxa-3,8,11-triazatetradec-1-ylcarbamate was prepared
 by a multistep procedure, which includes the reaction of intermediate
 tert-Bu (1S,2S,4R)-4-amino-1-benzyl-2-hydroxy-5-[4-(2-
 pyridinyl)phenyl]pentylcarbamate with N-protected L-tert-leucine. Compds.
 of the invention showed EC50 values 0.7-300 nM against wild-type HIV.
 IT 192725-55-6P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (preparation of amino acid derivs. as HIV protease inhibitors)
 RN 192725-55-6 HCAPLUS
 CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl
 ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:14172 HCAPLUS

DOCUMENT NUMBER: 142:114047

TITLE: A preparation of furofuranyl derivative, useful as inhibitor of HIV aspartyl protease

INVENTOR(S): Roberts, John Charles; Toczko, Jennifer Fell

PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; Martin, Michael Tolar

SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000249	A2	20050106	WO 2004-US20353	20040625
WO 2005000249	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1638960	A2	20060329	EP 2004-777060	20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2007521277	T	20070802	JP 2006-517643	20040625
US 2006148865	A1	20060706	US 2005-560500	20051212
PRIORITY APPLN. INFO.:			US 2003-483002P	P 20030627
			WO 2004-US20353	W 20040625

OTHER SOURCE(S): CASREACT 142:114047

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

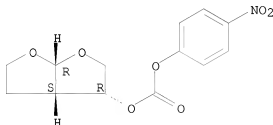
AB The invention relates to a preparation of furofuranyl derivative I, useful as inhibitor of HIV aspartyl protease (no biol. data). For instance, I was prepared via deprotection of II and coupling with III with a yield of 90% (example 2).

IT 192725-55-6P
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:534173 HCAPLUS

DOCUMENT NUMBER: 141:89016

TITLE: Preparation of benzimidazolylazabicyclooctylethylpiperidine
 s as Ccr5 antagonists for the treatment of HIV
 infection

INVENTOR(S): Kazmierski, Wieslaw Mieczyslaw; Aquino, Christopher
 Joseph; Bifulco, Neil; Boros, Eric Eugene; Chauder,
 Brian Andrew; Chong, Pek Yoke; Duan, Maosheng; Deanda,
 Felix, Jr.; Koble, Cecilia Suarez; Mclean, Ed
 Williams; Peckham, Jennifer Poole; Perkins, Angilique
 C.; Thompson, James Benjamin; Vanderwall, Dana

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; et al.; et al.

SOURCE: PCT Int. Appl., 859 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054974	A2	20040701	WO 2003-US39644	20031212
WO 2004054974	A3	20040902		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
 NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,

	TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW	
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,	
	BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,	
	ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,	
	TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	
CA 2509711	A1 20040701	CA 2003-2509711 20031212
AU 2003300902	A1 20040709	AU 2003-300902 20031212
EP 1569646	A2 20050907	EP 2003-813419 20031212
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,	
	IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK	
BR 2003017230	A 20051025	BR 2003-17230 20031212
CN 1744899	A 20060308	CN 2003-80109628 20031212
JP 2006511554	T 20060406	JP 2004-560838 20031212
NO 2005002739	A 20050819	NO 2005-2739 20050607
US 2006229336	A1 20061012	US 2005-538144 20050609
MX 2005PA06354	A 20050826	MX 2005-PA6354 20050613
IN 2005KN01328	A 20060630	IN 2005-KN1328 20050711
ZA 2005005600	A 20060927	ZA 2005-5600 20050712
PRIORITY APPLN. INFO.:		US 2002-433634P P 20021213
		WO 2003-US39644 W 20031212
OTHER SOURCE(S):	MARPAT 141:89016	
GI		

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Compds. I [R1 = (optionally substituted) alkyl, aryl, heteroaryl, carbocyclyl; R2 = H, (optionally substituted) alkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, aralkyl, heteroarylalkyl, heteroarylalkyl, aralkylcarbonyl, heteroarylalkyl; R3 = H, halo, cyano, trifluoromethyl, (optionally substituted) amino, acylamino, alkyl; X = C1-5 alkylene, optionally substituted with oxo or thioxo groups or halogen atoms, and optionally containing 1-3 oxygen, nitrogen, sulfur, or phosphorus atoms; Y = carbonyl, thiocarbonyl, 1,2-dioxoethylene, oxyalkylcarbonyl, sulfinyl, sulfonyl, oxycyanoimino, (optionally substituted) aminocarbonyl, carbonylamino, aminothiocarbonyl, oxyiminomethyl, thioiminomethyl, amino(cyanoimino)methyl, (cyanoimino)methyl, amino(acylimino)methyl, amino(sulfonylimino)methyl, amino(sulfinylimino)methyl, amino(alkoxyimino)methyl, amino(imino)methyl, (cyanoimino)methoxy, iminomethoxy, (cyanoimino)methanethiyl, alkylcarbonyloxy; A = saturated, partially saturated, or aromatic monocyclic ring with 5-6 atoms or a bicyclic ring with 8-10 members containing 0-5 nitrogen, oxygen, and/or sulfur atoms] such as II are prepared I are prepared as Ccr5 antagonists for the treatment of viral infections, (particularly HIV infection), related syndromes such as AIDS-related complex (ARC), progressive generalized lymphadenopathy, Kaposi's sarcoma, and neurol. conditions, and other diseases such as multiple sclerosis, rheumatoid arthritis, Crohn's disease, and immune-mediated disorders. The invention compds. have pIC50 values of ≥ 5 in assays for Ccr5 antagonism. Piperidineacetaldehyde III is prepared in four steps from 4-phenyl-4-piperidinecarbonitrile by protection of the piperidine with Boc anhydride, reduction of the nitrile with diisobutylaluminum hydride, Wittig olefination with methoxymethylphosphonium chloride, and hydrolysis of the enol ether with catalytic p-toluenesulfonic acid monohydrate. The

hydrochloride of endo-(benzimidazolyl)azabicyclooctane IV is prepared in five steps from tert-Bu endo-3-oxo-8-azabicyclo[3.2.1]octane-8-carboxylate; reductive amination with benzylamine, reductive cleavage of the benzyl group by palladium-mediated hydrogenation, a nucleophilic aryl substitution reaction with 1-fluoro-2-nitrobenzene, reduction of the nitro group by hydrogenation over palladium on carbon, and treatment with tri-Et orthoacetate followed by treatment with hydrochloric acid in ethanol. Coupling of III and IV by reductive amination with sodium triacetoxyborohydride, cleavage of the Boc group with hydrochloric acid in dioxane, and acylation with pivaloyl chloride and triethylamine yields II.

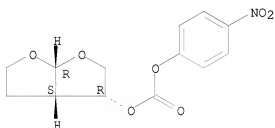
IT 192725-55-6

RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of benzimidazolylazabicyclooctylethylpiperidine Ccr5 antagonists in the treatment of bacterial and viral infections and other diseases)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:99287 HCAPLUS

DOCUMENT NUMBER: 140:339141

TITLE: Novel arylsulfonamides possessing sub-picomolar HIV protease activities and potent anti-HIV activity

against wild-type and drug-resistant viral strains
AUTHOR(S): Miller, John F.; Furfine, Eric S.; Hanlon, Mary H.; Hazen, Richard J.; Ray, John A.; Robinson, Laurence; Samano, Vicente; Spaltenstein, Andrew

CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(4), 959-963

CODEN: BMCLE8; ISSN: 0960-894X

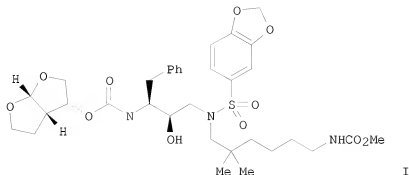
PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 140:339141

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AB Furanofuryl analogs of the HIV protease inhibitor amprenavir such as I are prepared in which a terminally substituted n-alkyl group is appended to the N-iso-Bu group of amprenavir and in which the substituents on the N-arylsulfonyl moiety are varied. Some of the inhibitors such as I are found to have greatly enhanced inhibition of HIV protease; the amprenavir analogs also inhibit the growth of both wild-type and resistant strains of HIV and are more effective against the HIV strains than the currently marketed HIV protease inhibitors amprenavir, indinavir, and nelfinavir. E.g., I inhibits wild-type HIV protease with a K_i value of 0.014 μM , and inhibits wild-type and resistant strains of HIV with IC_{50} values of between 1.6 nM and 15 nM.

IT 192725-55-6P

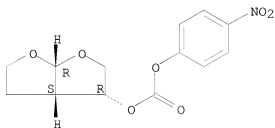
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of furanofuryl amprenavir analogs with modifications at the N-arylsulfonyl and N-iso-Bu moieties which show improved HIV protease inhibition and inhibition of wild-type and resistant HIV strains)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:875072 HCAPLUS

DOCUMENT NUMBER: 139:381610

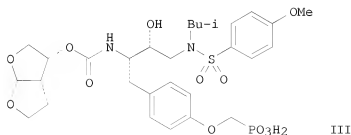
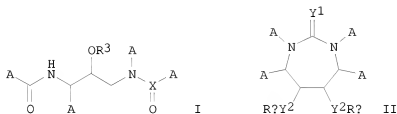
TITLE: Preparation of phosphonate analogs of HIV protease

inhibitors and methods for identifying anti-HIV
therapeutic compounds
INVENTOR(S): Birkus, Gabriel; Chen, James M.; Chen, Xiaowu; Cihlar,
Tomas; Eisenberg, Eugene J.; Hatada, Marcos; He,
Gong-Xin; Kim, Choung U.; Lee, William A.; McDermott,
Martin J.; Swaminathan, Sundaramoorthi
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 814 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003090691	A2	20031106	WO 2003-US12943	20030425
WO 2003090691	A3	20060209		
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CN 1649885	A	20050803	CN 2003-814963	20030425
CN 1656109	A	20050817	CN 2003-812478	20030425
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AT 367394	T	20070815	AT 2003-747326	20030425
CN 101041669	A	20070926	CN 2006-10154203	20030425
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WO 2004096818	A2	20041111	WO 2003-EP12423	20031106
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EP 1620445	A2	20060201	EP 2003-767521	20031106
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JP 2006524487	T	20061102	JP 2004-571244	20031106
US 2005239054	A1	20051027	US 2003-740694	20031222

US 2005136397	A1	20050623	US 2004-970389	20041022
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ZA 2004009376	A	20050914	ZA 2004-9376	20041122
ZA 2004009377	A	20060329	ZA 2004-9377	20041122
US 2006115815	A1	20060601	US 2005-511183	20050223
US 2007190523	A1	20070816	US 2007-554287	20070212
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			US 2002-375665P	P 20020426
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			WO 2003-US12901	A 20030425
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			WO 2003-US12943	W 20030425
			US 2003-513532P	P 20031024
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			US 2003-514894P	P 20031029
			US 2003-514925P	P 20031029
			WO 2003-EP12423	W 20031106
			WO 2004-US35083	A 20041022

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AB The invention relates to phosphonate-substituted carbamates I and cyclic

ureas II [wherein A = A1, A2, or W3 with the proviso that at least one of A = A1; A1 = [Y2(CR2R2)1-12]0-12Y2W6; A2 = [Y2(CR2R2)1-12]0-12Y2W3; W3 = substituted (hetero)cyclyl, R5, C(Y1)R5, C(Y1)W5, SO2R5, or SO2W5; W5 = substituted (hetero)cyclyl; W6 = triphosphono-substituted W3; Y1 = O, S, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), or N(N(Rx)2); Y2 = independently a bond, O, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), N(N(Rx)2), SO0-2, or SO0-2SO0-2; Rx = independently H, R1, W3, a protecting group, etc.; R1 = independently H or alkyl; R2 = independently H, R1, halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SO-2Rx, substituted alkyl, alkenyl, alkynyl, etc.; R3 = halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SRx, SO2Rx, OC(Y1)Rx, OC(Y1)ORx, C(Y1)Rx, etc. with provisos; R5 = substituted alkyl, alkenyl, or alkynyl; or pharmaceutically acceptable salts, hydrates, and formulations thereof] and other phosphonate-substituted analogs of HIV protease inhibitors for treating AIDS and other antiviral infections, as well as for use in assays for the detection of HIV protease. Compds. of the invention inhibit reverse transcriptase activity and have improved intracellular half-life compared to analogs not having the phosphonate or phosphonate prodrug. Libraries of such compds. were screened optionally using the novel enzyme GS-7340 ester hydrolase. Compns. and methods relating to GS-7340 ester hydrolase also are provided. Examples include preps. for non-nucleoside phosphonate protease inhibitors. In addition, extensive biol. data regarding PBMC uptake and metabolism, serum stability, and alkaline phosphatase protease inhibitor (ALPPI) activity of selected phosphonate-substituted prodrugs is presented. For instance, a 9-step reaction sequence starting from N-tert-butoxycarbonyl-O-benzyl-L-tyrosine provided III (K1 ≤10 pM for ALPPI activity). The synthesis involved multiple protection and deprotection steps along with coupling reactions using isobutylamine, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-2-yl 4-nitrophenyl carbonate, and dibenzyl hydroxymethylphosphonate.

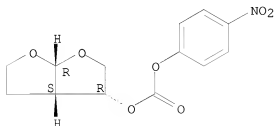
IT 192725-55-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phosphonate-substituted HIV protease inhibitors for treatment of AIDS and other viral infections)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:875071 HCAPLUS

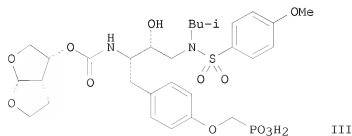
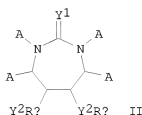
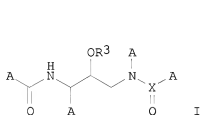
DOCUMENT NUMBER: 139:381609

TITLE: Preparation of phosphonate analogs of HIV protease inhibitors with improved cellular accumulation

properties
 INVENTOR(S): Arimilli, Murty N.; Becker, Mark M.; Bryant, Clifford; Chen, James M.; Chen, Xiaowu; Dastgah, Azar; Fardis, Maria; He, Gong-Xin; Jin, Haolun; Kim, Choung U.; Lee, William A.; Lee, Christopher P.; Lin, Kuei-Ying; Liu, Hongtao; Mackman, Richard L.; Mitchell, Michael L.; Nelson, Peter H.; Pyun, Hyung-Jung; Rowe, Tanisha D.; Sparacino, Mark; Swaminathan, Sundaramoorthi; Tario, James D.; Wang, Jianying; Williams, Matthew A.; Xu, Lianhong; Yang, Zheng-Yu; Yu, Richard H.; Zhang, Jiancun; Zhang, Lijun
 PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
 SOURCE: PCT Int. Appl., 1727 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 9
 PATENT INFORMATION:

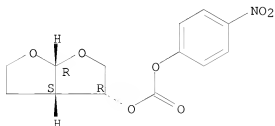
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003090690	A2	20031106	WO 2003-US12901	20030425
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EP 1620445	A2 20060201	EP 2003-767521 20031106
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US 2005239054	A1 20051027	US 2003-740694 20031222
IN 2004DN03045	A 20070413	IN 2004-DN3045 20041005
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		WO 2003-US12901 W 20030425
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OTHER SOURCE(S):	MARPAT 139:381609	
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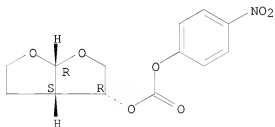
- AB The invention relates to phosphonate-substituted carbamates I and cyclic ureas II [wherein A = A1, A2, or W3 with the proviso that at least one of A = A1; A1 = [Y2(CR2R2)1-12]0-12Y2W6; A2 = [Y2(CR2R2)1-12]0-12Y2W3; W3 = substituted (hetero)cyclyl, R5, C(Y1)R5, C(Y1)W5, SO2R5, or SO2W5; W5 = substituted (hetero)cyclyl; W6 = triphosphono-substituted W3; Y1 = O, S, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), or N(N(Rx)2); Y2 = independently a bond, O, N(Rx), N(O)(Rx), N(ORx), N(O)(ORx), N(N(Rx)2), SOO-2, or SOO-2SOO-2; Rx = independently H, R1, W3, a protecting group, etc.; R1 = independently H or alkyl; R2 = independently H, R1, halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SO-2Rx, substituted alkyl, alkenyl, alkynyl, etc.; R3 = halo, CN, N3, NO2, Y1, Rx, N(Rx)2, SRx, SORx, SO2Rx, OC(Y1)Rx, OC(Y1)ORx, C(Y1)Rx, etc. with provisos; R5 = substituted alkyl, alkenyl, or alkynyl; or pharmaceutically acceptable salts, hydrates, and formulations thereof] and other phosphonate-substituted analogs of HIV protease inhibitors for treating AIDS and other antiviral infections, as well as for use in assays for the detection of HIV protease. Comps. of the invention inhibit reverse transcriptase activity and have improved intracellular half-life compared to analogs not having the phosphonate or phosphonate prodrug. Examples include preps. for non-nucleoside saquinavir-like, lopinavir-like, ritonavir-like, indinavir-like, atazanavir-like, nefinavir-like, tipranavir-like, amprenavir-like, KNI-like, and cyclic carbonyl-like phosphonate protease inhibitors. In addition, extensive biol. data regarding PBMC uptake and metabolism, serum stability, and alkaline phosphatase protease inhibitor (ALPPI) activity of selected phosphonate-substituted prodrugs is presented. For instance, a 9-step reaction sequence starting from N-tert-butoxycarbonyl-O-benzyl-L-tyrosine provided III (Ki ≤ 10 pM for ALPPI activity). The synthesis involved multiple protection and deprotection steps along with coupling reactions using isobutylamine, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-2-yl 4-nitrophenyl carbonate, and dibenzyl hydroxymethylphosphonate.
- IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phosphonate-substituted HIV protease inhibitors for treatment of AIDS and other viral infections)
- RN 192725-55-6 HCAPLUS
- CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



DOCUMENT NUMBER: 140:41969
 TITLE: Synthesis and SAR studies of potent HIV protease inhibitors containing novel dimethylphenoxyl acetates as P2 ligands
 AUTHOR(S): Chen, Xiaoli; Kempf, Dale J.; Li, Lin; Sham, Hing L.; Vasavanonda, Sudthida; Wideburg, Norman E.; Saldivar, Ayda; Marsh, Kennan C.; McDonald, Edith; Norbeck, Daniel W.
 CORPORATE SOURCE: Pharmaceutical Products Division, Abbott Laboratories, Abbott Park, IL, 60064, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(21), 3657-3660
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 140:41969
 AB Iso-Pr substituted 4-thioazolyl valine side chains are highly optimized P2-P3 ligands for C2 symmetry-based HIV protease inhibitors, as exemplified by the drug ritonavir. Replacement of the side chain with the conformationally constrained hexahydrofurofuranloxy P2 ligand in combination with a dimethylphenoxylacetate on the other end of the ritonavir core diamine yielded highly potent HIV protease inhibitors. The in vitro antiviral activity in MT4 cells increased by 10- and 20-fold, resp., in the absence and presence of 50% human serum compared to ritonavir. The structure-activity relationships of inhibitor series with this combination of ligands were investigated. Preliminary pharmacokinetic studies in rats indicated rapid elimination of the inhibitors from the blood, and the plasma levels were not significantly enhanced by coadministration with ritonavir. However, the novel structural features and the high intrinsic antiviral potency of this series provides potential for the future exploration of prodrug strategies.
 IT 192725-55-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation and structure-activity relationship of potent HIV protease inhibitor containing novel dimethylphenoxyl acetates as P2 ligands)
 RN 192725-55-6 HCAPLUS
 CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

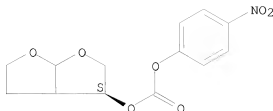


REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2000:699185 HCAPLUS
 DOCUMENT NUMBER: 133:267150
 TITLE: Preparation of amino acid sulfonamide derivatives as inhibitors of aspartyl protease
 INVENTOR(S): Tung, Roger Dennis; Salituro, Francesco Gerald; Deininger, David D.; Murcko, Mark Andrew; Novak, Perry Michael; Bhisetti, Govinda Rao
 PATENT ASSIGNEE(S): Vertex Pharmaceuticals, Incorporated, USA
 SOURCE: U.S., 74 pp., Cont.-in-part of U.S. Ser. No. 207,580, abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6127372	A	20001003	US 1996-424372	19960401
WO 9524385	A1	19950914	WO 1995-US2420	19950224
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1994-207580	B2 19940307
			WO 1995-US2420	W 19950224
OTHER SOURCE(S): MARPAT 133:267150				
AB	Sulfonamides Z-(CH-D)pC(:G)(CXX')mC(:G')N(D')SO ₂ -E' [Z = N(D), SO ₂ E, NH-A, N(D)-A, NH-E, NHC(O)N(D)(E), NH-Ht, N(D)-Ht or phthalimidyl (A = Ht or -R1-Ht, where Ht is a heterocycle which may be substituted, R1 = CO, SO ₂ , COCO, O ₂ C, OSO ₂ , NHSO ₂ , NHCO, NHCOCO, which may be substituted); D, D' = aryl, carbocycle, Ht, alkyl, alkenyl, cycloalkyl, cycloalkenyl, etc.; m = 1-3; p = 0 or 1; G, G' = H ₂ or O; X, X' = H, OH, NH ₂ , SH, D, halo or XX' = O] were prepared as aspartyl protease inhibitors. Thus, t-BuNHCON(CH ₂ Ph)CH ₂ CH(OH)N(CH ₂ -cyclopentyl)SO ₂ C ₆ H ₄ OMe-p, prepared by sequential reactions of cyclopentylmethylamine, p-methoxybenzenesulfonyl chloride, epibromohydrin, benzylamine, and t-Bu isocyanate, showed Ki = 2,400 for inhibition of HIV-1 protease.			
IT	298206-05-0 RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of amino acid sulfonamide derivs. as inhibitors of aspartyl protease)			
RN	298206-05-0 HCAPLUS			
CN	Carbonic acid, (3S)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)			

Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2008 ACS on SIN

ACCESSION NUMBER: 2000:573770 HCAPLUS

DOCUMENT NUMBER: 133:177157

TITLE: Preparation of [1-benzyl-2-hydroxy-3-(arylsulfonamido)propyl]carbamates as HIV aspartyl protease inhibitors

INVENTOR(S): Hale, Michael R.; Baker, Christopher T.; Stammers, Timothy A.; Sherrill, Ronald G.; Spaltenstein, Andrew; Furfine, Eric S.; Maltais, Francois; Andrews, Clarence Webster, III; Miller, John F.; Samano, Vicente

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 369 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

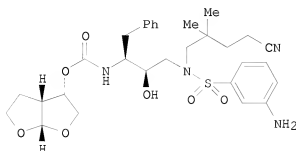
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000047551	A2	20000817	WO 2000-US3288	20000209
WO 2000047551	A3	20010816		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6319946	B1	20011120	US 2000-500781	20000209
EP 1159278	A2	20011205	EP 2000-913402	20000209
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002536430	T	20021029	JP 2000-598472	20000209
AT 311391	T	20051215	AT 2000-913402	20000209
EP 1637518	A2	20060322	EP 2005-25977	20000209
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
ES 2254156	T3	20060616	ES 2000-913402	20000209
PT 1159278	T	20060630	PT 2000-913402	20000209
TW 260322	B	20060821	TW 2000-89102108	20000209
US 2002198388	A1	20021226	US 2001-927271	20010809

US 6617350	B2	20030909	US 2003-613650	20030702
US 2004127488	A1	20040701	US 1999-120047P	P 19990212
PRIORITY APPLN. INFO.:			SY 2000-1090	A 20000207
			EP 2000-913402	A3 20000209
			US 2000-500781	A3 20000209
			WO 2000-US3288	W 20000209
			US 2001-927271	A3 20010809

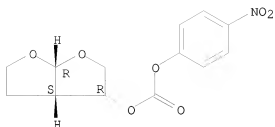
OTHER SOURCE(S): MARPAT 133:177157
GI



I

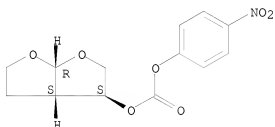
- AB ABxN(Gx)CH(D)CH(OR7)CH2ND'E'E [wherein A = H, or (un)substituted Ht, R1Ht, or R1Ak; Ak = alkyl; Ht = cycloalkyl, cycloalkenyl, or (un)substituted aryl or heterocyclyl; R1 = CO(CO), (O)SO2, O2C, or (un)substituted NHSO2 or NHCO(CO); B = (un)substituted NHCH2CO; x = 0 or 1; G = H, R7, alkyl; or G may be bound to R7 to form a heterocyclic ring; R7 = H, (CH2O)xY(ZM)(:X)Z(M)x; etc.; M = H, Li, Na, K, Mg, Ca, Ba, alkyl, alkenyl, etc.; X = O or S; Y = P or S; Z = H, O, S, or (un)substituted NH2; D = independently Q or (un)substituted (cyclo)alkyl or (cyclo)alkenyl; Q = (un)substituted carbocyl or heterocyclyl; D' = (un)substituted alkyl, alkenyl, alkynyl; E = Ht, OHt, HtHt, alkoxy, (un)substituted NH2, alkyl, or carbocyl; E' = CO or SO2] were prepared as antiviral agents against HIV-1 and HIV-2 viruses. Thus, 3-NO2C6H4SO2Cl was added to tert-Bu (1S,2R)-N-[1-benzyl-3-[(4-cyano-2,2-dimethylbutyl)amino]-2-hydroxypropyl]carbamate (preparation given) to form the 3-nitrophenylsulfonamide (55%). Reduction to the 3-aminophenylsulfonamide (85%), followed by transesterification with [(3S,3aR,6aS)-hexahydrofuro[2,3-b]furan-3-yl](4-nitrophenyl)carbonate (65%), gave I. In an antiviral activity assay, I inhibited HIV-1 protease in the MT4 cell line with Ki < 1 nM and IC50 < 0.1 μM.
- IT 192725-55-6 252873-01-1 252873-35-1
252873-51-1 288296-64-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of heterocyclyl
arylsulfonamidopropylcarbamate HIV protease inhibitors by reductive
alkylation of amines and subsequent addition of arylsulfonyl chlorides)
- RN 192725-55-6 HCAPLUS
- CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl
ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



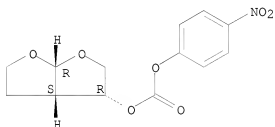
RN 252873-01-1 HCAPLUS
 CN Carbonic acid, (3S,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



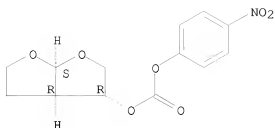
RN 252873-35-1 HCAPLUS
 CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester, rel- (CA INDEX NAME)

Relative stereochemistry.



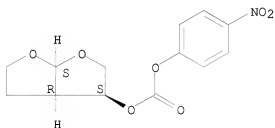
RN 252873-51-1 HCAPLUS
 CN Carbonic acid, (3R,3aR,6aS)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



RN 288296-64-0 HCAPLUS
 CN Carbonic acid, (3S,3aR,6aS)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



L15 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2008 ACS on SIN

ACCESSION NUMBER: 1999:811207 HCAPLUS

DOCUMENT NUMBER: 132:49801

TITLE: Preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-hydroxypropanes and related compounds as inhibitors of HIV aspartyl protease.

INVENTOR(S): Sherrill, Ronald George; Hale, Michael R.; Spaltenstein, Andrew; Furfine, Eric Steven; Andrews, Clarence Webster, III; Lowen, Gregory Thomas

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 344 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965870	A2	19991223	WO 1999-US13744	19990617
WO 9965870	A3	20010315		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,				

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2335477	A1	19991223	CA 1999-2335477	19990617
AU 9945760	A	20000105	AU 1999-45760	19990617
AU 767728	B2	20031120		
EP 1086076	A1	20010328	EP 1999-928769	19990617
EP 1086076	B1	20041222		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, FI

BR 9912169	A	20010410	BR 1999-12169	19990617
NZ 508855	A	20031031	NZ 1999-508855	19990617
AT 285396	T	20050115	AT 1999-928769	19990617
PT 1086076	T	20050531	PT 1999-928769	19990617
ES 2235492	T3	20050701	ES 1999-928769	19990617
AP 1717	A	20070228	AP 2000-2023	19990617
US 2002049201	A1	20020425	US 2000-731129	20001206
US 6613743	B2	20030902		
NO 2000006405	A	20010219	NO 2000-6405	20001215
MX 2000PA12637	A	20010405	MX 2000-PA12637	20001218
HK 1037605	A1	20051007	HK 2001-106764	20010925
US 2004097594	A1	20040520	US 2003-600937	20030620
NZ 528074	A	20041126	NZ 2003-528074	20030908
AU 2004200636	A1	20040311	AU 2004-200636	20040219
US 2006172936	A1	20060803	US 2005-212045	20050825
AU 2007234578	A1	20071213	AU 2007-234578	20071121

PRIORITY APPLN. INFO.: P 19980619
 WO 1999-US13744 W 19990617
 US 2000-731129 A3 20001206
 US 2003-600937 B3 20030620
 AU 2004-200636 A3 20040219

OTHER SOURCE(S): MARPAT 132:49801

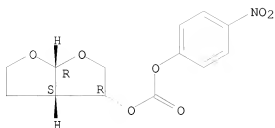
AB ABxN(Gx)CHDCHOR7CH2ND'SO2E [A = H, (substituted) Ht, R1Ht, R1Ak; Ak = alkyl; Ht = cycloalkyl, cycloalkenyl, (substituted) aryl, heterocyclyl; R1 = CO, SO2, COCO, O2C, NR2CO, NR2SO2, etc.; B = null, NR2C(R3)2CO; x = 0, 1; R2 = H, (substituted) Ht, alkyl; R3 = H, (substituted) Ht, alkyl, alkenyl, cycloalkyl, cycloalkenyl; G = null, H, R7, alkyl; G may be bound to R7; D = (substituted) Q, alkyl, alkenyl; Q = (substituted) carbocyclyl, heterocyclyl; D' = OR10, N:R10, N(R10)R1R3; E = Ht, OHT, OR3, NR2R3, (substituted) alkyl, alkenyl, etc.; R7 = H, (CH2O)xY(ZM)(:X)Z(M)x, etc.; M = null, H, Li, Na, K, Mg, Ca, Ba, alkyl, alkenyl, etc.; X = O, S; Y = P, S; Z = O, S, N(R2)2, H], were prepared as inhibitors of HIV aspartyl protease (no data). Thus, 3-H2NC6H4SO2NHOCHMe2 (preparation given), tert-Bu N-(1S)-1-[(2S)-oxiran-2-yl]-2-phenylethylcarbamate, and phosphazene base P4 tert-Bu were stirred in 8 h in THF to give 95% tert-Bu N-(1S,2R)-3-[[[(3-aminophenyl)sulfonyl](isopropoxy)amino]-1-benzyl-2-hydroxypropylcarbamate.

IT 192725-55-6 252873-35-1 252873-40-8
 252873-51-1
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-hydroxypropanes and related compds. as inhibitors of HIV aspartyl protease)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

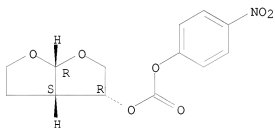
Absolute stereochemistry. Rotation (-).



RN 252873-35-1 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester, rel- (CA INDEX NAME)

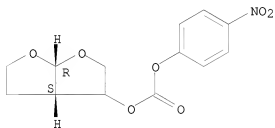
Relative stereochemistry.



RN 252873-40-8 HCAPLUS

CN Carbonic acid, (3aR,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

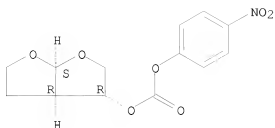
Absolute stereochemistry.



RN 252873-51-1 HCAPLUS

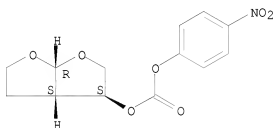
CN Carbonic acid, (3R,3aR,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



IT 252873-01-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-
 hydroxypropanes and related compds. as inhibitors of HIV aspartyl
 protease)
 RN 252873-01-1 HCAPLUS
 CN Carbonic acid, (3S,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl
 ester (CA INDEX NAME)

Absolute stereochemistry.

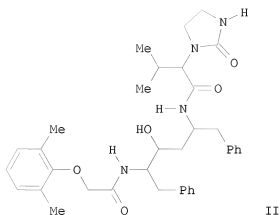


L15 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1999:393986 HCAPLUS
 DOCUMENT NUMBER: 131:59143
 TITLE: Preparation of peptide analogs as retroviral protease
 inhibitors
 INVENTOR(S): Sham, Hing Leung; Norbeck, Daniel W.; Chen, Xiaohui;
 Betebenner, David A.
 PATENT ASSIGNEE(S): Abbott Laboratories, USA
 SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 572,226,
 abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5914332	A	19990622	US 1996-753201	19961121
CA 2238978	A1	19970619	CA 1996-2238978	19961206
CA 2238978	C	20010515		

CA 2285119	A1	19970619	CA 1996-2285119	19961206
CA 2285119	C	20050920		
CA 2509505	A1	19970619	CA 1996-2509505	19961206
WO 9721685	A1	19970619	WO 1996-US20440	19961206
W: AU, CA, CN, CZ, HU, IL, JP, KR, MX, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9713422	A	19970703	AU 1997-13422	19961206
AU 725369	B2	20001012		
EP 882024	A1	19981209	EP 1996-944941	19961206
EP 882024	B1	20020206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
CN 1208405	A	19990217	CN 1996-199904	19961206
HU 9901079	A2	19990928	HU 1999-1079	19961206
HU 223782	B1	20050128		
JP 2000502085	T	20000222	JP 1997-522278	19961206
JP 3170292	B2	20010528		
HU 20003305	A3	20001228	HU 2000-3305	19961206
HU 222731	B1	20030929		
JP 2001058979	A	20010306	JP 2000-190510	19961206
EP 1170289	A2	20020109	EP 2001-124290	19961206
EP 1170289	A3	20021113		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
AT 212986	T	20020215	AT 1996-944941	19961206
PT 882024	T	20020731	PT 1996-944941	19961206
ES 2173341	T3	20021016	ES 1996-944941	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
NZ 510329	A	20040227	NZ 1996-510329	19961206
CZ 293650	B6	20040616	CZ 2000-2210	19961206
CZ 294246	B6	20041110	CZ 1998-1762	19961206
NZ 510328	A	20050128	NZ 1996-510328	19961206
IL 156237	A	20050517	IL 1996-156237	19961206
NZ 338003	A	20050826	NZ 1996-338003	19961206
CZ 296915	B6	20060712	CZ 2004-762	19961206
ZA 9610475	A	19970731	ZA 1996-10475	19961212
TW 494097	B	20020711	TW 1997-86101654	19970213
TW 259178	B	20060801	TW 2000-89115157	19970213
US 6284767	B1	20010904	US 1998-207873	19981208
HK 1016585	A1	20020809	HK 1999-101462	19990409
US 6313296	B1	20011106	US 2000-511390	20000223
US 2002004503	A1	20020110	US 2001-837280	20010418
US 6472529	B2	20021029		
US 2003100755	A1	20030529	US 2002-280652	20021025
US 7279582	B2	20071009		
PRIORITY APPLN. INFO.:				
			US 1995-572226	B2 19951213
			US 1996-753201	A 19961121
			US 1996-754687	A 19961121
			CA 1996-2238978	A3 19961206
			CA 1996-2285119	A3 19961206
			EP 1996-943605	A3 19961206
			EP 1996-944941	A3 19961206
			IL 1996-124607	A3 19961206
			JP 1997-522278	A3 19961206
			WO 1996-US20440	W 19961206
			US 1998-207873	A3 19981208
			US 2001-837280	A3 20010418

OTHER SOURCE(S): MARPAT 131:59143
GI



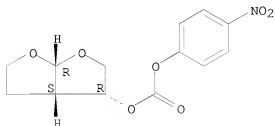
AB R4Z1CONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [I; R1,R2 = lower alkyl, cycloalkylalkyl, arylalkyl; R3 = lower alkyl, hydroxyalkyl, cycloalkylalkyl; R4 = aryl, heterocyclyl; R5 = N-attached (thi)oxo- or iminoazacycloalkyl; Z1 = Z, O, S, (alkyl)imino, OZ, ZO, NHZ, etc.; Z = alkylene] were prepared Thus, title compound (S,S,S)-II was prepared in 8 steps from L-phenylalanine. Data for biol. activity of I were given.

IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:515728 HCAPLUS
DOCUMENT NUMBER: 127:122001

TITLE: Preparation of peptide analogs as retroviral protease inhibitors

INVENTOR(S): Sham, Hing Leung; Norbeck, Daniel W.; Chen, Xiaohu; Betebenner, David A.; Kempf, Dale J.; Herrin, Thomas R.; Kumar, Gondi N.; Condon, Stephen L.; Cooper, Arthur J.; Dickman, Daniel A.; Hannick, Steven M.; Kolaczowski, Lawrence; Oliver, Patricia A.; Plata, Daniel J.; Stengel, Peter J.; Stoner, Eric J.; Tien, Jieh-Heh J.; Liu, Jih-Hua; Patel, Ketan M.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: PCT Int. Appl., 180 pp.
CODEN: PIXXD2

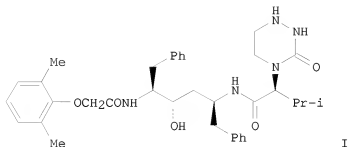
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

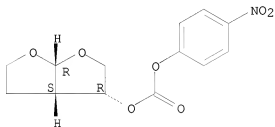
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721685	A1	19970619	WO 1996-US20440	19961206
W: AU, CA, CN, CZ, HU, IL, JP, KR, MX, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5914332	A	19990622	US 1996-753201	19961121
AU 9713422	A	19970703	AU 1997-13422	19961206
AU 725369	B2	20001012		
EP 882024	A1	19981209	EP 1996-944941	19961206
EP 882024	B1	20020206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
HU 9901079	A2	19990928	HU 1999-1079	19961206
HU 223782	B1	20050128		
JP 2000502085	T	20000222	JP 1997-522278	19961206
JP 3170292	B2	20010528		
HU 20003305	A3	20001228	HU 2000-3305	19961206
HU 222731	B1	20030929		
AT 212986	T	20020215	AT 1996-944941	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
IL 156237	A	20050517	IL 1996-156237	19961206
HK 1016585	A1	20020809	HK 1999-101462	19990409
PRIORITY APPLN. INFO.:			US 1995-572226	A 19951213
			US 1996-753201	A 19961121
			US 1996-754687	A 19961121
			EP 1996-943605	A3 19961206
			IL 1996-124607	A3 19961206
			WO 1996-US20440	W 19961206
OTHER SOURCE(S):		MARPAT 127:122001		
GI				



- AB R4 -L1-CONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [R1, R2 = lower alkyl, cycloalkylalkyl, arylalkyl; R3 = lower alkyl, hydroxyalkyl, cycloalkylalkyl; R4 = aryl, heterocyclyl; R5 = heterocyclyl e.g. Q - Q4; wherein m, n = 1-3; p = 1,2; X = O, S, NH; Y = CH2, O, S, (un)substituted NH; Z = O, S, NH; L1 = O, S, (un)substituted NH, O-alkylenyl, S(O)m-alkylenyl (wherein m = 0, 1,2), N-(un)substituted NH-alkylenyl, alkylenyl, alkenylenyl, etc.] are prepared Methods and compns. for inhibiting an HIV infection are also disclosed. Thus, (2S)-(4-benzoyloxycarbonylaza-1-tetrahydropyrimid-2-onyl)-3-methylbutanoic acid (preparation given) was condensed with (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-amino-1,6-diphenylhexane using standard coupling procedure [1-ethyl-3-(3-dimethylaminopropyl)carbodiimide/DMF] followed by hydrogenolysis over 10% Pd-C to give the title compound (I). I in vitro at 0.5 nmol inhibited HIV protease by 94.6%.
- IT 192725-55-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)
- RN 192725-55-6 HCAPLUS
- CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L15 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:515727 HCAPLUS

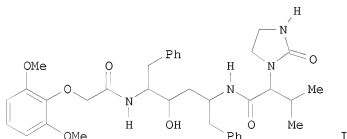
DOCUMENT NUMBER: 127:121994

TITLE: Preparation and formulation of N-(α -aminoacyl)diaminoalcohols as HIV protease inhibitors

INVENTOR(S): Sham, Hing Leung; Stewart, Kent D.; Kempf, Dale J.
 PATENT ASSIGNEE(S): Abbott Laboratories, USA
 SOURCE: PCT Int. Appl., 163 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721683	A1	19970619	WO 1996-US19394	19961206
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2238977	A1	19970619	CA 1996-2238977	19961206
EP 876353	A1	19981111	EP 1996-943605	19961206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000502997	T	20000314	JP 1997-522112	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1995-572226	A 19951213
			US 1996-754687	A 19961121
			EP 1996-943605	A3 19961206
			WO 1996-US19394	W 19961206

OTHER SOURCE(S): MARPAT 127:121994
 GI



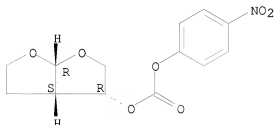
- AB R4ZCONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [I; R1,R2 = (cyclo)alkyl, aralkyl; R3 = (cyclo)alkyl, hydroxyalkyl; R4 = heterocyclyl or aryl; R5 = N-attached oxoheterocyclyl, etc.] were prepared. Thus, (S)-(PhCH2)2NCH(CH2Ph)COCH2CN (preparation given) was condensed with PhCH2MgCl and the product reduced by NaBH4 to give (S,S,S)-(PhCH2)2NCH(CH2Ph)CH(OH)CH2CH(NH2)CH2Ph. The latter was N-protected and the N-debenzylated product amidated by 2,6-(MeO)C6H3OCH2CO2H (preparation given) to give, after deprotection and amidation by (S)-Me2CHCHR5CO2H (R5 = 2-oxo-1H-imidazol-3-yl) (preparation given), title compound (S,S,S,S)-II. Data for biol. activity of I were given.
- IT 192725-55-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and formulation of N-(α -aminoacyl)diaminoalcohols as HIV protease inhibitors)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



=> d ibib abs hitstr 1-34 114

L14 ANSWER 1 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1207559 HCAPLUS

DOCUMENT NUMBER: 147:502107

TITLE: Preparation of 2-({4-chloro-2-[(3-chloro-5-cyanophenyl)carbonyl]phenyl}oxy)-N-(4-[(2S)-2,3-dihydroxy-3-methylbutyl]oxy)-2-methylphenyl)acetamide as a non-nucleoside reverse transcriptase inhibitor

INVENTOR(S): Aquino, Christopher Joseph; Freeman, George Andrew; Martin, Michael Tolar

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCI Int. Appl., 34pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

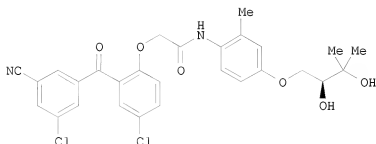
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007121415	A2	20071025	WO 2007-US66733	20070417
WO 2007121415	A3	20071221		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				

PRIORITY APPLN. INFO.: US 2006-792496P P 20060417

GI



I

AB The present invention relates to a compound I that is a non-nucleoside reverse transcriptase inhibitor, and to processes for the preparation and use of the same. I was prepared in a multi-step synthesis, starting from (2S)-2,3-dihydroxy-3-methylbutyl 4-methylbenzenesulfonate. Specifically, the present invention includes methods of using compound I in the treatment of human immunodeficiency virus infection. I was tested against wild type and clin. relevant HIV (IC50 data were given). Pharmaceutical composition comprising the compound I alone and in combination with other therapeutic agents are disclosed.

IT 313682-08-5

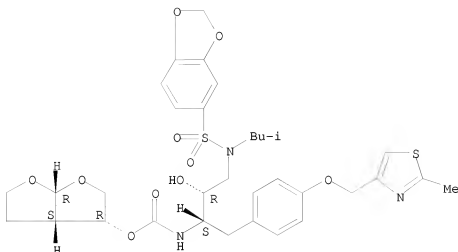
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of 2-(phenylcarbonylphenoxy)-N-(dihydroxymethylbutoxyphenyl)acetamide as non-nucleoside reverse transcriptase inhibitors useful in combination therapy of HIV infection)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1207558 HCAPLUS

DOCUMENT NUMBER: 147:502106

TITLE: Preparation of 2-({4-chloro-2-[(3-chloro-5-cyanophenyl)carbonyl]phenyl}oxy)-N-{3-fluoro-4-[(2-hydroxy-2-methylpropyl)oxy]-2-methylphenyl}acetamide as a non-nucleoside reverse transcriptase inhibitor
Aquino, Christopher Joseph; Freeman, George Andrew; Martin, Michael Tolar

INVENTOR(S): Smithkline Beecham Corporation, USA

PATENT ASSIGNEE(S): PCT Int. Appl., 27pp.

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

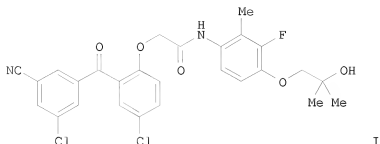
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007121418	A2	20071025	WO 2007-US66736	20070417
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2006-792543P P 20060417
US 2006-863846P P 20061101

GI



AB The present invention relates to a compound I that is a non-nucleoside reverse transcriptase inhibitor, and to processes for the preparation and use of the same. I was prepared in a multi-step synthesis, starting from (2,3-difluoro-6-nitrophenyl)acetic acid. Specifically, the present invention includes methods of using compound I in the treatment of human immunodeficiency virus infection. I was tested against wild type and clin. relevant HIV (IC₅₀ data were given). Pharmaceutical composition comprising the compound I alone and in combination with other therapeutic agents are disclosed.

IT 313682-08-5, Brecanavir

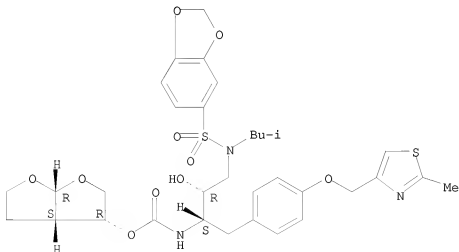
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of 2-(phenylcarbonylphenoxy)-N-(hydroxypropoxyphenyl)acetamide as non-nucleoside reverse transcriptase inhibitors useful in combination therapy of HIV infection)

RN 313682-08-5 HCAPLUS

CN Carbanic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1207557 HCAPLUS

DOCUMENT NUMBER: 147:502105

TITLE: Preparation of 2-((4-chloro-2-((3-chloro-5-cyanophenyl)carbonyl)phenyl)oxy)-N-((4-((2,3-dihydroxy-3-methylbutyl)oxy)-3-fluoro-2-methylphenyl)acetamide as a non-nucleoside reverse transcriptase inhibitor

INVENTOR(S): Aquino, Christopher Joseph; Freeman, George Andrew; Martin, Michael Tolar

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 36pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

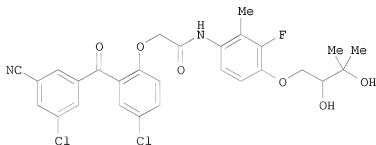
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007121416	A2	20071025	WO 2007-US66734	20070417
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2006-792434P P 20060417
US 2006-863846P P 20061101

GI



I

AB The present invention relates to a compound I that is a non-nucleoside reverse transcriptase inhibitor, and to processes for the preparation and use of the same. Compds. (2S)-I, (2R)-I and rac-I were prepared. For example, I was prepared in a multi-step synthesis, starting from (2,3-difluoro-6-nitrophenyl)acetic acid. Specifically, the present invention includes

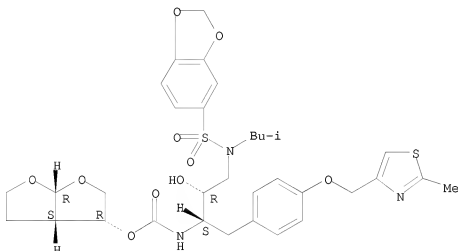
methods of using compound I in the treatment of human immunodeficiency virus infection. (2S)-I, (2R)-I and rac-I were tested against wild type and clin. relevant HIV (IC50 data were given). Pharmaceutical composition comprising the compound I alone and in combination with other therapeutic agents are disclosed.

IT 313682-08-5
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of 2-(phenylcarbonylphenoxy)-N-(hydroxymethylbutoxyphenyl)acetamide as non-nucleoside reverse transcriptase inhibitor useful in combination therapy of HIV infection)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)-(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1075740 HCAPLUS

DOCUMENT NUMBER: 147:495981

TITLE: Potent Inhibition of HIV-1 Replication by Novel Non-peptidyl Small Molecule Inhibitors of Protease Dimerization

AUTHOR(S): Koh, Yasuhiro; Matsumi, Shintaro; Das, Debananda; Amano, Masayuki; Davis, David A.; Li, Jianfeng; Leschenko, Sofiya; Baldridge, Abigail; Shioda, Tatsuo; Yarchoan, Robert; Ghosh, Arun K.; Mitsuya, Hiroaki

CORPORATE SOURCE: Department of Hematology, Kumamoto University Graduate School of Medical and Pharmaceutical Sciences, Honjo, 860-8556, Japan

SOURCE: Journal of Biological Chemistry (2007), 282(39), 28709-28720

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular

DOCUMENT TYPE: Biology
 LANGUAGE: Journal
 English

AB Dimerization of HIV-1 protease subunits is essential for its proteolytic activity, which plays a critical role in HIV-1 replication. Hence, the inhibition of protease dimerization represents a unique target for potential intervention of HIV-1. The authors developed an intermol. fluorescence resonance energy transfer-based HIV-1-expression assay employing cyan and yellow fluorescent protein-tagged protease monomers. Using this assay, the authors identified nonpeptidyl small mol. inhibitors of protease dimerization. These inhibitors, including darunavir and two exptl. protease inhibitors, blocked protease dimerization at concns. of as low as 0.01 μ M and blocked HIV-1 replication with IC₅₀ values of 0.0002-0.48 μ M. These agents also inhibited the proteolytic activity of mature protease. Other approved anti-HIV-1 agents examined except tipranavir, a CCR5 inhibitor, and soluble CD4 failed to block the dimerization event. Once protease monomers dimerize to become mature protease, mature protease is not dissociated by this dimerization inhibition mechanism, suggesting that these agents block dimerization at the nascent stage of protease maturation. The proteolytic activity of mature protease that managed to undergo dimerization despite the presence of these agents is likely to be inhibited by the same agents acting as conventional protease inhibitors. Such a dual inhibition mechanism should lead to highly potent inhibition of HIV-1.

IT 313682-08-5, Brecanavir

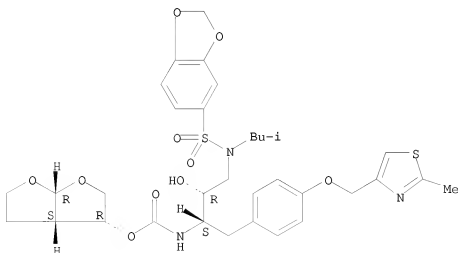
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(potent inhibition of HIV-1 replication by novel non-peptidyl small mol. inhibitors of protease dimerization)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1064150 HCAPLUS

DOCUMENT NUMBER: 147:385768

TITLE: Diketo acids with nucleobase scaffolds: anti-HIV replication inhibitors targeted at HIV integrase in combination therapy

INVENTOR(S): Nair, Vasu; Chi, Guochen; Uchil, Vinod R.

PATENT ASSIGNEE(S): University of Georgia Research Foundation, Inc., USA

SOURCE: PCT Int. Appl., 110pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

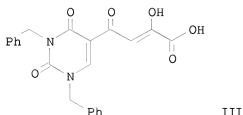
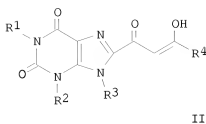
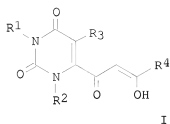
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007106450	A2	20070920	WO 2007-US6245	20070309
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2006-781520P P 20060310

OTHER SOURCE(S): CASREACT 147:385768; MARPAT 147:385768

GI



AB A new class of diketo acids constructed on nucleobase scaffolds, e.g., I [R1, R2 = (un)substituted CH2Ph whereby Ph is substituted with 1 to 3 substituents selected from halogen, OH, OMe, Me, Et, Pr, CF3, CH2Rb; Rb = 5- or 6-membered heteroarom.; R3 = H, C1-6-alkyl, halogen, (un)substituted CH2Ph, (un)substituted SPh, whereby Ph is substituted with 1 to 3 substituents selected from halogen, OH, OMe, Me, Et, Pr, CF3; R4 = CO2R; R = H, C1-6-alkyl] and II, designed as inhibitors of HIV replication through inhibition of HIV integrase, is described. Thus, 4-(1,3-dibenzyl-1,2,3,4-tetrahydro-2,4-dioxypyrimidin-5-yl)-2-hydroxy-4-oxo-2-butenic acid (III) was prep'd from 5-acetyluracil via dibenylation with PhCH2Br in DMF containing K2CO3, condensation with MeO2CCO2Me in THF containing NaOCMe3, and acid hydrolysis with aqueous HCl in dioxane. These compds. are useful in the prevention or treatment of infection by HFV and in the treatment of AIDS and ARC, either as the compds., or as pharmaceutically acceptable salts, with pharmaceutically acceptable carriers, in combination with antivirals, immunomodulators, antibiotics, vaccines, and other therapeutic agents, especially other anti-HIV compds. (including other anti-HIV integrase agents), which can be used to create combination anti- HIV cocktails as disclosed herein. Methods of treating AIDS and ARC and methods of treating or preventing infection by HIV are also described. Compds. of the present application include those of I and include tautomers, regioisomers, geometric isomers, and where applicable, optical isomers thereof, and pharmaceutically acceptable salts thereof, wherein the nucleobase scaffold and R groups are as otherwise defined in the specification. These are combined with any number of typical other anti-HIV agents to provide an effective treatment modality for HIV infections, including AIDS and ARC. The bioactivity of III was determined [IC50 = 0.02 μ M; CC50 = >2000 μ M; Therapeutic Index = >10,000 vs. HIV integrase *in vitro*].

IT 313682-08-5, BrecaNavir

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

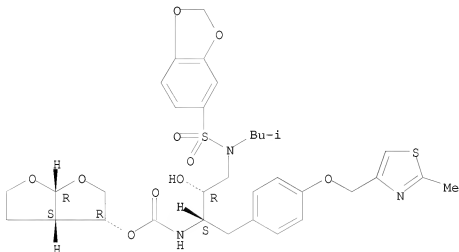
(novel diketo acids constructed on nucleobase scaffolds as inhibitors

of HIV replication through inhibition of HIV integrase useful in prevention and combination therapy of infections)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1021139 HCAPLUS

DOCUMENT NUMBER: 147:335724

TITLE: In vitro antiviral activity of the novel, tyrosyl-based human immunodeficiency virus (HIV) type 1 protease inhibitor brecanavir (GW640385) in combination with other antiretrovirals and against a panel of protease inhibitor-resistant HIV
AUTHOR(S): Hazen, Richard; Harvey, Robert; Ferris, Robert; Craig, Charles; Yates, Phillip; Griffin, Philip; Miller, John; Kaldor, Istvan; Ray, John; Samano, Vincente; Furfine, Eric; Spaltenstein, Andrew; Hale, Michael; Tung, Roger; St. Clair, Marty; Hanlon, Mary; Boone, Lawrence

CORPORATE SOURCE: Metabolic and Viral Diseases CEDD, Department of Virology, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA

SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(9), 3147-3154

CODEN: AMACQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Brecanavir, a novel tyrosyl-based arylsulfonamide, high-affinity, human immunodeficiency virus type 1 (HIV-1) protease inhibitor (PI), has been evaluated for anti-HIV activity in several in vitro assays. Preclin.

assessment of breacanavir indicated that this compound potently inhibited HIV-1 in cell culture assays with 50% effective concns. (EC50s) of 0.2 to 0.53 nM and was equally active against HIV strains utilizing either the CXCR4 or CCR5 coreceptor, as was found with other PIs. The presence of up to 40% human serum decreased the anti-HIV-1 activity of breacanavir by 5.2-fold, but under these conditions the compound retained single-digit nanomolar EC50s. When breacanavir was tested in combination with nucleoside reverse transcriptase inhibitors, the antiviral activity of breacanavir was synergistic with the effects of stavudine and additive to the effects of zidovudine, tenofovir, dideoxycytidine, didanosine, adefovir, abacavir, lamivudine, and emtricitabine. Breacanavir was synergistic with the nonnucleoside reverse transcriptase inhibitor nevirapine or delavirdine and was additive to the effects of efavirenz. In combination with other PIs, breacanavir was additive to the activities of indinavir, lopinavir, nelfinavir, ritonavir, amprenavir, saquinavir, and atazanavir. Clin. HIV isolates from PI-experienced patients were evaluated for sensitivity to breacanavir and other PIs in a recombinant virus assay. Breacanavir had a <5-fold increase in EC50s against 80% of patient isolates tested and had a greater mean in vitro potency than amprenavir, indinavir, lopinavir, atazanavir, tipranavir, and darunavir. Breacanavir is by a substantial margin the most potent and broadly active antiviral agent among the PIs tested in vitro.

IT 313682-08-5, GW 640385

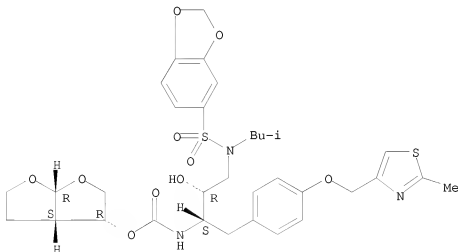
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(in vitro antiviral activity of tyrosyl-based HIV-1 protease inhibitor breacanavir (GW640385) in combination with other antiretrovirals and against panel of protease inhibitor-resistant HIV)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

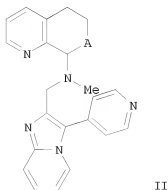
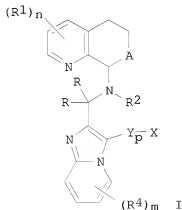
L14 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:845883 HCAPLUS
 DOCUMENT NUMBER: 147:235169
 TITLE: Imidazo[1,2-a]pyridine-3-carboxamides as anti-HIV agents and their preparation, pharmaceutical compositions and their use in monotherapy and in combination therapy of diseases
 INVENTOR(S): Gudmundsson, Kristjan; Turner, Elizabeth Madalena
 PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA; Svolto, Angilique Christina
 SOURCE: PCT Int. Appl., 104pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007/087548	A2	20070802	WO 2007-US60938	20070124
WO 2007/087548	A9	20070927		
WO 2007/087548	A3	20071213		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

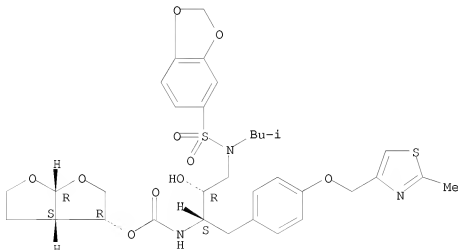
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: MARPAT 147:235169 US 2006-761883P P 20060125
 OTHER SOURCE(S):
 GI



- AB The invention provides compds. of formula I including salts, solvates, and pharmaceutically acceptable derivs. thereof, pharmaceutical formulations containing them, processes for their preparation, and methods of treatment using them. Compds. of formula I wherein A is (CH₂)₀₋₂; each R is independently H, C1-8 (halo)alkyl, C2-8 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, etc.; each R1 is independently halo, C1-8 (halo)alkyl, C2-8 alkenyl, C2-6 alkynyl, C3-8 cycloalkyl, C3-8 cycloalkenyl, etc.; n and m are independently 0, 1 and 2; R2 is H, C1-8 (halo)alkyl, C3-8 cycloalkyl, C2-6 alkenyl, C2-6 alkynyl, etc.; p is 0 and 1; Y is NH and derivs., O, CONH and derivs., NHCO and derivs., CO, CO₂, NHCONH and derivs., S, SO, SO₂, etc.; X is (un)substituted (hetero)arylamine, (un)substituted (hetero)aryl, (un)substituted heterocyclyl, etc.; R4 is halo, C1-8 (halo)alkyl, C2-6 alkenyl, C2-6 alkynyl, C2-8 cycloalkyl, OH and derivs., CN, NO₂, etc.; and their pharmaceutically acceptable derivs. thereof, are claimed. Example compound II was prepared by a multistep procedure (procedure given). All the invention compds. were evaluated for their anti-HIV activity. From the assay, it was determined that the tested compds. exhibited IC₅₀ values of about 1 nM to about 50 μ M.
- IT 313682-08-5, BrecaNAVIR
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (codrug; preparation of imidazopyridinecarboxamides as anti-HIV agents useful in monotherapy and in combination therapy of diseases)
- RN 313682-08-5 HCAPLUS
- CN Carbanic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



DOCUMENT NUMBER: 147:132968
 TITLE: Preliminary safety and efficacy data of brecaonavir, a novel HIV-1 protease inhibitor: 24 week data from study HPR10006
 AUTHOR(S): Lalezari, Jacob P.; Ward, Douglas J.; Tomkins, Susan A.; Garges, Harmony P.
 CORPORATE SOURCE: Quest Clinical Research, Department of Medicine, University of California at San Francisco, San Francisco, CA, USA
 SOURCE: Journal of Antimicrobial Chemotherapy (2007), 60(1), 170-174
 CODEN: JACHDX; ISSN: 0305-7453
 PUBLISHER: Oxford University Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

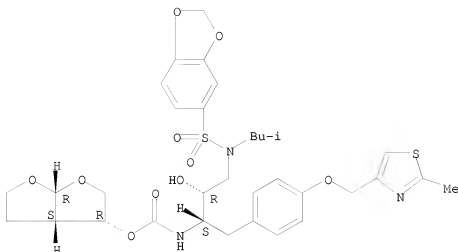
AB Brecaonavir, a novel protease inhibitor (PI), has sub-nM in vitro antiviral activity against multi-PI-resistant HIV-1 and in vitro is >100-fold more potent than previously marketed PIs and approx. 10-fold more potent than the recently marketed PI, darunavir. HPR10006 is an open label, single-arm, descriptive 48 wk study, with 8 and 24 wk interim analyses. Thirty-one HIV-1-infected patients were enrolled and received brecaonavir/ritonavir 300 mg/100 mg twice daily, with two nucleoside reverse transcriptase inhibitors, based on history and genotype. At baseline, 25/31 had PI-sensitive virus and 6/31 had PI-resistant virus (median of two primary PI and five secondary PI mutations). Median baseline HIV-1 RNA was 5.0 and 4.2 log10 copies/mL, resp. Four patients discontinued prior to Week 24. At Week 24, 77% (24/31) had HIV-1 RNA <50 copies/mL regardless of screening genotype, including 5/6 patients with PI-resistant virus (6/6 had HIV-1 RNA <400 copies/mL). Brecaonavir/ritonavir was well tolerated with no serious adverse events or clin. concerning changes in laboratory parameters. Of 31 patients, 10 (32%) experienced drug-related Grade 2-4 adverse events [most frequent events were fatigue (13%), dyspepsia (10%) and nausea (10%)]. Baseline isolate brecaonavir IC50 values for all patients ranged from 0.1 to 0.2 nM. Median plasma trough concentration at Week 4 was 150 ng/mL. Correcting the IC50 (0.2 nM) value for protein binding (6-fold increase in vitro with 50% human serum) gives a corrected inhibitory quotient of 180. Brecaonavir/ritonavir was well tolerated and showed potent antiviral activity in HIV-1-infected patients harbouring both PI-sensitive and PI-resistant virus, following 24 wk of dosing.

IT 313682-08-5, Brecaonavir
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (HIV-1 protease inhibitor brecaonavir safety and efficacy)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)-(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:642553 HCAPLUS

DOCUMENT NUMBER: 147:72745

TITLE: Preparation of novel spiropiperidine compounds for the modulation of chemokine receptor activity

INVENTOR(S): Moinet, Christophe; Courchesne, Marc

PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.

SOURCE: PCT Int. Appl., 81pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

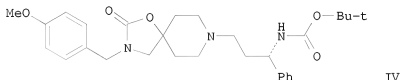
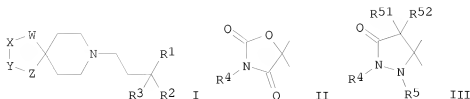
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007065256	A1	20070614	WO 2006-CA1981	20061205
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2005-742545P P 20051206

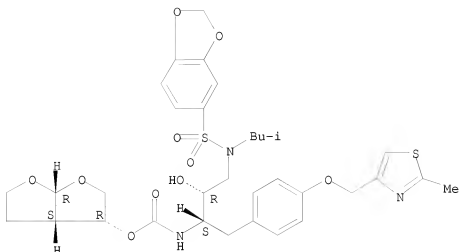
OTHER SOURCE(S): MARPAT 147:72745

GI



- AB The title compds. I [ring containing W, X, Y and Z = II, III, etc.; R1 = NR6C(O)R7, NR6C(O)OR7, etc.; R2 = alkyl, alkenyl, aryl, etc.; R3 = H, alkyl, aryl; R4, R5, R51, R52 = H, alkyl, aryl, etc.; R6 = H, alkyl, alkenyl, alkynyl; R7 = H, alkyl, alkenyl, aryl, etc.], useful for the modulation of CCR5 chemokine receptor activity, particularly in the prevention or treatment of inflammatory diseases, immunoregulatory diseases, organ transplantation reactions and infectious diseases such as HIV infections, were prepared and claimed. E.g., a multi-step synthesis of (S)-IV, starting from tert-Bu 2-oxo-1-oxa-3,8-diaza-spiro[4.5]decane-8-carboxylate and 4-methoxybenzyl chloride, was given. Compds. I have been found to have activity in binding to the CCR5 receptor, generally with an IC50 value of less than 25 μ M. Certain compds. I have also been tested in an assay for HIV activity and generally having an IC50 value of less than 1 μ M.
- IT 313682-08-5
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (codrug; preparation of novel spiroperididine compds. as chemokine receptor modulators useful in treatment and prevention of diseases)
- RN 313682-08-5 HCAPLUS
- CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:437040 HCAPLUS

DOCUMENT NUMBER: 146:394423

TITLE: Safety and pharmacokinetics of brecanavir, a novel human immunodeficiency virus type 1 protease inhibitor, following repeat administration with and without ritonavir in healthy adult subjects
 AUTHOR(S): Reddy, Y. Sunila; Ford, Susan L.; Anderson, Maggie T.; Murray, Sharon C.; Ng-Cashin, Judith; Johnson, Mark A.
 CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, USA
 SOURCE: Antimicrobial Agents and Chemotherapy (2007), 51(4), 1202-1208

CODEN: AMACCQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

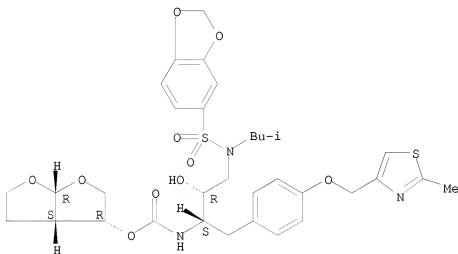
AB Brecanavir (BCV) is a novel, potent protease inhibitor in development for the treatment of human immunodeficiency virus (HIV-1) infection with low nM in vitro 50% inhibitory concns. (IC50s) against many multiprotease inhibitor resistant viruses. This study was a double-blind, randomized, placebo-controlled repeat-dose escalation to evaluate the safety, tolerability, and pharmacokinetics of BCV, with or without ritonavir (RTV), in 68 healthy subjects. Seven sequential cohorts (n = 10) received BCV (50 to 600 mg) in combination with 100 mg RTV (every 12 h [q12h] or q24h) or alone at 800 mg q12h for 15 days. BCV alone or in combination with RTV was well tolerated, with no serious adverse events reported. The most common drug-related adverse event was headache. BCV was readily absorbed with median time to maximum concentration of drug in serum values ranging from 2.5 to 5.0 h postdose following single- and repeat-dose administration of BCV alone and BCV with RTV 100 mg. Geometric mean BCV accumulation ratios ranged from 1.4 to 1.56 following BCV-RTV q24h regimens and from 1.84 to 4.93 following BCV q12h regimens. BCV steady

state was generally achieved by day 13 in all groups. All day 15 BCV-RTV trough concentration values in q12h regimens reached or surpassed the estimated protein-binding corrected in vitro IC50 target BCV concentration of 28 ng/mL for highly resistant isolates. The pharmacokinetic and safety profile of BCV-RTV supports continued investigation in HIV-1-infected subjects.

IT 313682-08-5, Brecanavir
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (HIV-1 antiviral brecanavir safety and pharmacokinetics: repeat administration with and without ritonavir in healthy humans)

RN 313682-08-5 HCAPLUS
 CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



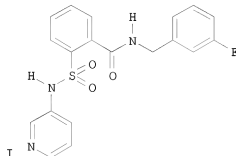
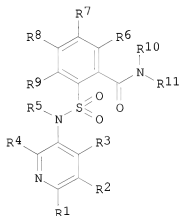
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:351992 HCAPLUS
 DOCUMENT NUMBER: 146:379833
 TITLE: Preparation of pyridinylaminosulfonylarylcarboxamides as cytochrome P450 3A4 inhibitors
 INVENTOR(S): Patterson, Brian Douglas; Sakata, Sylvie Kim; Nambu, Mitchell David; Patel, Leena Bharat Kumar; Tatlock, John Howard
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA
 SOURCE: PCT Int. Appl., 154pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007034312	A2	20070329	WO 2006-IB2639	20060911
WO 2007034312	A3	20070823		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
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US 2007167497	A1	20070719	US 2007-621410	20070109
PRIORITY APPLN. INFO.:			US 2005-720151P	P 20050923
			US 2005-723115P	P 20051003
			US 2005-725469P	P 20051011
			US 2006-762256P	P 20060125
			US 2006-821664P	P 20060807
			WO 2006-IB2639	A1 20060911

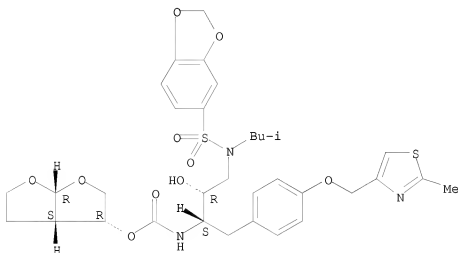
OTHER SOURCE(S): MARPAT 146:379833
GI



AB Title compds. I [R1-4 independently = H, alkyl, haloalkyl, etc.; R5 = H or alkyl; R6-9 independently = H, (un)substituted alkyl, heterocycloalkyl, etc.; R10 and R11 independently = H, (un)substituted alkyl, aryl, arylalkyl, etc.], and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of cytochrome P 450 3A4. Thus, e.g., II was prepared by condensation of Me 2-(chlorosulfonyl)benzoate with 3-pyridinamine followed by amidation with 3-fluorobenzylamine. Assays were described for determining Kiapp of I against recombinant CYP3A4 enzyme, e.g., II was determined to have a Kiapp = 0.269 (μM). Further disclosed are methods for the use of I and pharmaceutical formulations comprising them.

IT 313682-08-5, Brecanavir
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
 (Biological study); USES (Uses)
 (codrug for therapeutic administration; preparation of
 pyridinylaminosulfonylarylcarboxamides as cytochrome P 450 3A4
 inhibitors)
 RN 313682-08-5 HCAPLUS
 CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)-(2-
 methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-
 thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-
 b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:350523 HCAPLUS
 DOCUMENT NUMBER: 146:351294
 TITLE: Methods for treating viral infections using polyamine
 analogs
 INVENTOR(S): McGrath, Michael S.; Hadlock, Kenneth G.
 PATENT ASSIGNEE(S): Pathologica, LLC, USA
 SOURCE: PCT Int. Appl., 58pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007035957	A2	20070329	WO 2006-US37378	20060925
WO 2007035957	A3	20070907		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP,
 KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,

MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
 RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

US 2007078187 A1 20070405 US 2006-535001 20060925

PRIORITY APPLN. INFO.: US 2005-719573P P 20050923

AB Methods for treating viral infections using polyamine analogs, including mitoguazone (MGBG), are provided. In these methods, polyamine analogs destroy macrophages that act as viral reservoirs, facilitating the destruction of the viruses that dwell within the macrophages. Examples of viral infections that may be treated with the methods include, but are not limited to, infections from human immunodeficiency viruses. These methods differ from previous methods of treatment using polyamine analogs, wherein the polyamine analogs were administered only as antitumor agents.

IT 313682-08-5, Brecanavir

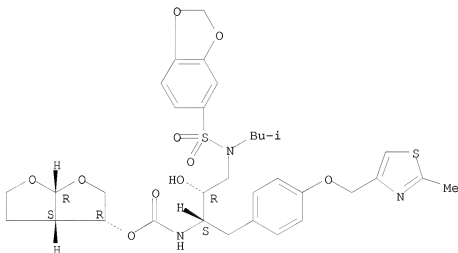
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(polyamine analogs for treatment of viral infections, and use with other agents)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl)methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:14210 HCAPLUS

DOCUMENT NUMBER: 146:121949

TITLE: Oxazolidinocarboxamides as HIV-1 protease inhibitors, and methods of making and using them

INVENTOR(S): Rana, Tariq M.; Ali, Akbar; Cao, Hong; Sai, Kiran
 Kuman Reddy Ga; Anjum, Saima Ghafoor
 PATENT ASSIGNEE(S): University of Massachusetts, USA
 SOURCE: PCT Int. Appl., 194pp., which which
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

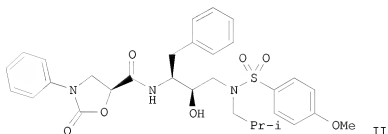
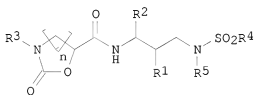
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007002173	A1	20070104	WO 2006-US24109	20060621

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-693134P P 20050622
 US 2005-749902P P 20051212
 US 2006-810234P P 20060602

OTHER SOURCE(S): MARPAT 146:121949
 GI



AB One aspect of the invention relates to the design, synthesis and biol. activity of novel HIV-1 protease inhibitors of incorporating N-phenyloxazolidinone-5-carboxamides into the (hydroxyethylamino)sulfonamide scaffold of formula I as P2 ligands. Compound of formula I wherein n is 1

and 2; R1 is OH, SH, and NH and derivs.; R2 is H, alkyl, cycloalkyl, (hetero)aryl, heterocyclyl(alkyl), and (hetero)aralkyl; R3 is H, alkyl, alkenyl, aminoalkyl, amidoalkyl, ketoalkyl, cycloalkyl, (hetero)aryl, etc.; R4 is alkyl, cycloalkyl, heterocyclyl(alkyl), (hetero)aryl, and (hetero)aralkyl; R5 is H, alkyl, cycloalkyl, heterocyclyl(alkyl), (hetero)aryl, and (hetero)aralkyl; and their stereochem. configurations at any undefined stereocenter is R, S, or a mixture of these configurations, are claimed. The invention relates to inhibitors with variations at the P2 phenyloxazolidine and the P2' phenylsulfonamide moieties. Remarkably, compds. with an (S)-enantiomer of substituted phenyloxazolidines at P2 show highly potent inhibitory activities against wild-type HIV-1 protease. In certain embodiments, the inhibitors of the invention have Ki values in low picomolar (pM) range. In certain embodiments, the inhibitors of the invention were shown to be active against a variety of multi-drug resistant (MDR) HIV-1 proteases, each representing different paradigm of drug resistance. Example compound II was prepared by a general coupling reaction using the corresponding sulfonamide. All the invention compds. were evaluated for their HIV-1 protease inhibitory activity (data given).

IT 313682-08-5, Brecanavir

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

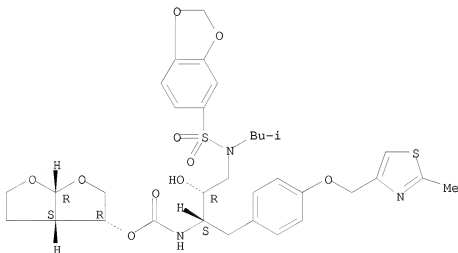
(Biological study); USES (Uses)

(codrug; preparation of oxazolidinecarboxamides as HIV-1 protease inhibitors useful as therapeutic agents)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:14194 HCAPLUS
 DOCUMENT NUMBER: 146:114998

TITLE: HIV-1 protease inhibitors
 INVENTOR(S): Schiffer, Celia; Rana, Tariq M.; Gilson, Michael;
 Tidor, Bruce
 PATENT ASSIGNEE(S): University of Massachusetts, USA
 SOURCE: PCT Int. Appl., 127pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007002172	A2	20070104	WO 2006-US24108	20060621
WO 2007002172	A3	20070405		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			

PRIORITY APPLN. INFO.: US 2005-693134P P 20050622
 OTHER SOURCE(S): MARPAT 146:114998
 AB Described are novel protease inhibitors and methods for using said protease inhibitors in the treatment of human immunodeficiency virus (HIV) infection.
 IT 313682-08-5, Brecanavir
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (HIV-1 protease inhibitors for treatment of human immunodeficiency virus infection and combination with other agents)
 RN 313682-08-5 HCAPLUS
 CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.

OTHER SOURCE(S): MARPAT 145:397501
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention features compds. of formula I that are HIV protease inhibitors and therefore are useful in the inhibition of HIV replication, the prevention and/or treatment of infection by HIV, and in the treatment of AIDS and/or ARC. Compds. of formula I wherein X is (un)substituted C1-5 alkylene; R1 is amino, C1-8 alkyl, C1-8 alkoxy, NR2, N(R2)2 and (un)substituted heterocycle; R2 is C1-8 alkyl and C1-8 alkoxy; and their pharmaceutically acceptable salts are claimed. Example compound II was prepared by in several steps (procedure given). All the invention compds. were evaluated for their HIV protease inhibitory activity. The key mean pharmacokinetic parameters, C_{max} and AUC_∞ values were determined to be < 1 ng/mL and < 1 ng/mL•hr, resp.

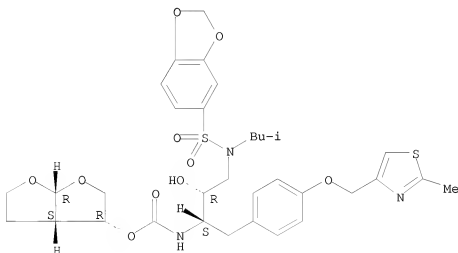
IT 313682-08-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of substituted carbamates as HIV protease inhibitors useful in treatment and prevention of HIV infection, AIDS and AIDS-related conditions)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



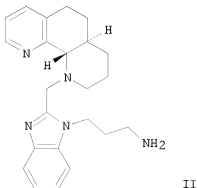
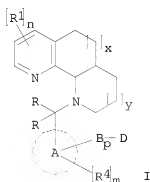
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:945669 HCAPLUS
 DOCUMENT NUMBER: 145:336055
 TITLE: Preparation of heteroarylmethyl substituted octahydro-1,10-phenanthrolines and analogs for treating diseases modulated by a chemokine receptor (CXCR4)
 INVENTOR(S): Gudmundsson, Kristjan; Catalano, John, G.; Svolto, Angilique
 PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
 SOURCE: PCT Int. Appl., 183pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

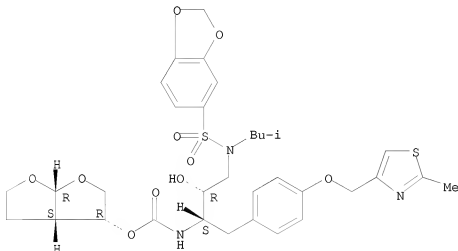
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006096444	A2	20060914	WO 2006-US7395	20060301
WO 2006096444	A3	20070927		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA EP 1853604 A2 20071114 EP 2006-736676 20060301 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
PRIORITY APPLN. INFO.:		US 2005-658530P	P	20050304
		WO 2006-US7395	W	20060301

OTHER SOURCE(S): MARPAT 145:336055
 GI



- AB The title compds. I [x, y = 0-2; R = H, alkyl, haloalkyl, etc.; n = 0-3; R1 = halo, haloalkyl, alkyl, etc.; A = heteroaryl; R4 = halo, haloalkyl, alkyl, etc.; m = 0-2; p = 0-1; B = O, CO, CO2, etc.; D = N(R10)2, (un)substituted 4-6 membered heterocyclyl or heteroaryl; R10 = H, alkyl, cycloalkyl, etc.], useful in the treatment of diseases and conditions caused by CXCR4, were prepared E.g., a multi-step synthesis of trans-II, starting from 6,7-dihydro-8(5H)-quinolinone and acrylonitrile, was given. Compound I were tested in the HIV-1 infectivity assay (IC50 of about 1 nM to about 50 μ M). Pharmaceutical formulations containing compds. I alone or in combination with other therapeutic agents are also disclosed.
- IT 313682-08-5, BrecaNavir
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of heteroarylmethyl substituted octahydro-1,10-phenanthrolines and their analogs for treating diseases modulated by a chemokine receptor (CXCR4))
- RN 313682-08-5 HCAPLUS
- CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)-(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



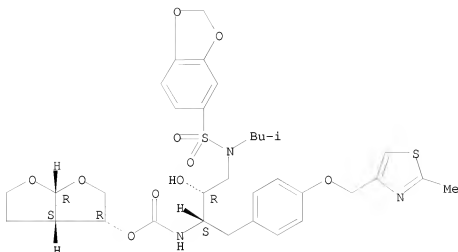
L14 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:722183 HCAPLUS
 DOCUMENT NUMBER: 145:240783
 TITLE: Inhibitors of HIV-1 protease: 10 years after
 AUTHOR(S): Mastrolorenzo, Antonio; Rusconi, Stefano; Scozzafava, Andrea; Supuran, Claudiu T.
 CORPORATE SOURCE: Dipartimento di Scienze Dermatologiche, Centro MTS, Universita degli Studi di Firenze, Florence, I-50121, Italy
 SOURCE: Expert Opinion on Therapeutic Patents (2006), 16(8), 1067-1091

CODEN: EOTPEG; ISSN: 1354-3776

PUBLISHER: Informa Healthcare
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

- AB A review. Highly active antiretroviral therapy (HAART) has dramatically changed the course of HIV infection. This therapy involves the use of at least three agents from two distinct classes of antivirals: a protease inhibitor (PI) in combination with two nucleoside/nucleotide reverse transcriptase inhibitors (N(t)RTIs); or a non-nucleoside reverse transcriptase inhibitor (NNRTI) in combination with NRTIs. Nine drugs containing PIs are clin. available: the first-generation saquinavir, ritonavir, indinavir, nelfinavir and amprenavir; and the second-generation fosamprenavir (the amprenavir prodrug), lopinavir, atazanavir and tipranavir. Many other compds. are in advanced clin. evaluation, such as darunavir (TMC-114) and brecanavir, among others. Many other effective HIV PIs were reported, mainly by using amprenavir and TMC-114 as lead mols. The main goals of research in this field are: (i) the design of better pharmacol. agents, devoid of severe side effects, resistance problems and with simple administration schedules (preferably once-daily); and (ii) achieving eradication of the virus and, possibly, a definitive cure of the disease. A review of the pharmacol. and interactions of these agents with other drugs is presented here, with emphasis on how these pharmacol. interferences may improve the clin. use of antivirals, or how side effects due to PI drugs may be managed better by taking them into account (e.g., ritonavir boosting of other PIs, which reduces dosages and administration schedules of these drugs). Except for being highly effective in the treatment of HIV infection, recent reports showed this class of drugs to be effective as antitumor agents, apoptosis enhancers, antibacterials (e.g., against Mycobacterium tuberculosis infection), antifungals (e.g., against Candida albicans), antimalarials, anti-SARS and anti-influenza agents.
- IT 313682-08-5, Brecanavir
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (inhibitors of HIV-1 protease and anti-AIDS therapy)
- RN 313682-08-5 HCAPLUS
- CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



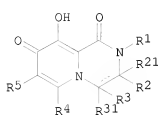
REFERENCE COUNT: 121 THERE ARE 121 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:633928 HCAPLUS
 DOCUMENT NUMBER: 145:103723
 TITLE: Preparation of hydroxydihydropyridopyrazine-1,8-diones for inhibiting HIV integrase
 INVENTOR(S): Chan Chun Kong, Laval; Liu, Bingcan; Nguyen-Ba, Nghe; Cadilhac, Caroline; Turcotte, Nathalie
 PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.
 SOURCE: PCI Int. Appl., 186 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

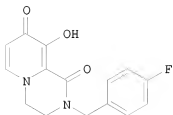
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006066414	A1	20060629	WO 2005-CA1964	20051222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2004-638180P P 20041223
 OTHER SOURCE(S): MARPAT 145:103723

GI



I



II

AB The title compds. I [R1 = H, OH, (un)substituted aryl, etc.; R2, R21, R3, R31 = H, (un)substituted alkyl, cycloalkyl, etc.; or two of R2, R21, R3 and R31 can be joined to form a condensed or spiro ring; or R2 and R21 or R3 and R31 can also be joined together to form a carbonyl; R4 = (un)substituted alkoxy, aryloxy, arylalkoxy; R5 = H, halo, OH, etc.], useful for preventing or treating human immunodeficiency virus (HIV) infection or for preventing, delaying or treating acquired immunodeficiency syndrome (AIDS), were prepared E.g., a multi-step synthesis of II, starting from 3-methoxy-2-methyl-1H-pyridone, was given. Compds. I have been found to have activity in the inhibition of HIV integrase, generally with an observed inhibitory activity at 50 μ M. Certain compds. I have also been tested in an assay for HIV activity and generally having an IC50 value of less than 10 μ M. Pharmaceutical compns. comprising the compound I alone or in combination with other therapeutic agents are disclosed.

IT 313682-08-5, VX 385

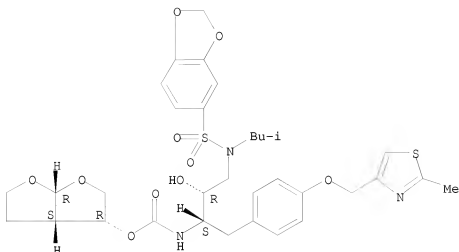
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of hydroxydihydropyridopyrazinediones as HIV integrase inhibitors for treating, preventing or delaying HIV infection and AIDS)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl)methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:578211 HCAPLUS

DOCUMENT NUMBER: 145:62897

TITLE: Preparation of spirotropane compounds and therapeutic use as modulators of chemokine receptor activity

INVENTOR(S): Chan Chun Kong, Laval; Moinet, Christophe; Courchesne, Marc; Vaillancourt, Louis; Blais, Charles; Bubenik, Monica

PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.

SOURCE: PCI Int. Appl., 145 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

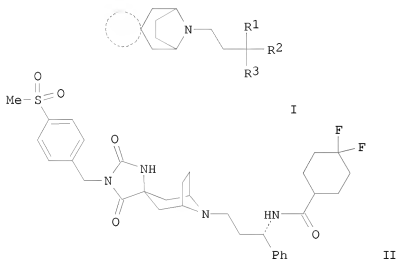
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060919	A1	20060615	WO 2005-CA1878	20051209
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
AU 2005313813	A1	20060615	AU 2005-313813	20051209
CA 2587508	A1	20060615	CA 2005-2587508	20051209

EP 1831222 A1 20070912 EP 2005-819431 20051209
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
 BA, HR, MK, YU
 CN 101098871 A 20080102 CN 2005-80046172 20051209
 IN 2007KN02150 A 20070817 IN 2007-KN2150 20070612
 KR 2007095310 A 20070928 KR 2007-715147 20070702
 PRIORITY APPLN. INFO.: US 2004-634266P P 20041209
 US 2005-693051P P 20050623
 WO 2005-CA1878 W 20051209
 OTHER SOURCE(S): CASREACT 145:62897; MARPAT 145:62897
 GI



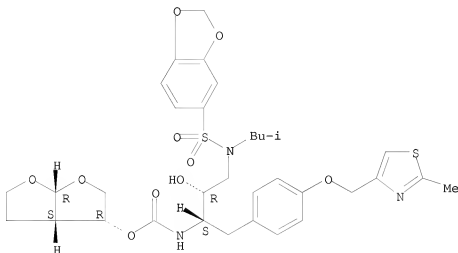
- AB Spiro compds. according to formula (I) are claimed: wherein R1 = NR7R9; R2 = (un)substituted C1-10 alkyl, C2-10 alkenyl, 3-10 membered heterocycle, etc.; R3 = H, (un)substituted C1-10 alkyl or C6-12 aryl; R7 = H, (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl; R9 = H or (un)substituted C1-10-alkyl; and ring A represents a 5 or 6 membered heteroring substituted once or twice with a keto substituent. These compds. and their pharmaceutical acceptable salts are used in combinations or in pharmaceutical compns. and are useful in the modulation of CCR5 chemokine receptor activity (no data given). I are useful in the prevention or treatment of certain inflammatory diseases, immunoregulatory diseases, organ transplantation reactions and in the prevention and treatment of infectious diseases such as HIV infections. Preparation of I is exemplified. For example, II was prepared from 4,4-difluorocyclohexanecarboxylic acid ((S)-3-oxo-1-phenylpropyl)amide and 3-(4-methanesulfonylbenzyl)bicyclo[3.2.1]-1a,3,8-triazaspiro[4.5]dodecan-2,4-dione hydrochloride (preparation given).
- IT 313682-08-5, VX 385
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (addnl. therapeutic agent; preparation of spirotropane compds. and

therapeutic use as modulators of chemokine receptor activity)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:558325 HCAPLUS

DOCUMENT NUMBER: 145:62894

TITLE: Preparation of spirotropane compounds and methods for the modulation of chemokine receptor activity to block cellular entry of HIV

INVENTOR(S): Chan Chun Kong, Laval; Moinet, Christophe; Courchesne, Marc; Vaillancourt, Louis; Bubenik, Monica

PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.

SOURCE: PCT Int. Appl., 153 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

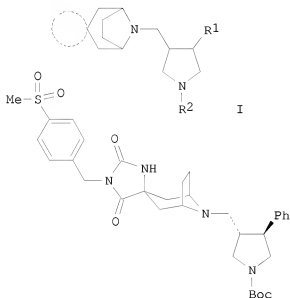
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060918	A1	20060615	WO 2005-CA1877	20051209
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,				

VN, YU, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM
 CA 2590737 A1 20060615 CA 2005-2590737 20051209
 EP 1824853 A1 20070829 EP 2005-819950 20051209
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,
 BA, HR, MK, YU

PRIORITY APPLN. INFO.: US 2004-634257P P 20041209
 WO 2005-CA1877 W 20051209

OTHER SOURCE(S): MARPAT 145:62894

GI



AB Comps. according to formula I (wherein the R1= (un)substituted alkyl, alkenyl, etc.; R2 = H, cycloalkylcarbonyl, ester, etc.; and A = a 5 or 6 membered heteroring involving a nitrogen or oxygen atom and one or two keto substituent) are claimed. These comps. and their pharmaceutical acceptable salt are used in combinations or pharmaceutical comps. and are useful in modulation of CCR5 chemokine receptor activity and blocking cellular entry of HIV (no biol. data given). Preparation of I is exemplified. For example, II was prepared from 3-(4-methanesulfonylbenzyl)bicyclo[3.2.1]-1a,3,8-triazaspiro[4.5]dodecan-2,4-dione hydrochloride (preparation given) and (3R,4S)-3-formyl-4-phenylpyrrolidine-1-carboxylic acid tert-Bu ester (preparation given).

II 313682-08-5, VX 385

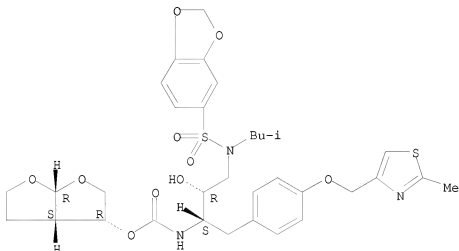
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(addnl. therapeutic agent; preparation of spirotropane compds. and methods for modulation of chemokine receptor activity to block cellular entry of HIV)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:547194 HCAPLUS

DOCUMENT NUMBER: 145:55430

TITLE: Single-dose safety and pharmacokinetics of brexanavir, a novel human immunodeficiency virus protease inhibitor

AUTHOR(S): Ford, Susan L.; Reddy, Y. Sunila; Anderson, Maggie T.; Murray, Sharon C.; Fernandez, Pedro; Stein, Daniel S.; Johnson, Mark A.

CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(6), 2201-2206

CODEN: AMACQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Brexanavir (BCV, 640385) is a novel, potent protease inhibitor (PI) with low nanomolar 50% inhibitory concns. against PI-resistant human immunodeficiency virus (HIV) in vitro. This phase I, double-blind, randomized, placebo-controlled, two-part single-dose study (first time with humans) was conducted to determine the safety, tolerability, and pharmacokinetics of BCV administered at 10 mg/mL in a tocopherol-polyethylene glycol succinate-polyethylene glycol 400-ethanol 50:40:10

solution. In part 1 of the study, single oral doses of BCV ranged from 25 mg to 800 mg. In part 2, single oral doses of BCV ranged from 10 mg to 300 mg and were coadministered with 100-mg oral ritonavir (RTV) soft gel capsules. Single doses of BCV and BCV/RTV were generally well tolerated. There were no severe adverse events (SAEs), and no subject was withdrawn due to BCV. The most commonly reported drug-related AEs during both parts of the study combined were gastrointestinal disturbances (similar to placebo) and headache. BCV was readily absorbed following oral administration with mean times to maximum concentration from >1 h to 2.5 h in

part 1

and from 1.5 h to 3 h in part 2. Administration of BCV without RTV resulted in BCV exposures predicted to be insufficient to inhibit PI-resistant virus based on in vitro data. Coadministration of 300 mg BCV with 100 mg RTV, however, significantly increased the plasma BCV area under the concentration-time curve and maximum concentration 26-fold and 11-fold, resp.,

achieving BCV concns. predicted to inhibit PI-resistant HIV.

IT 313682-08-5, Brexanavir

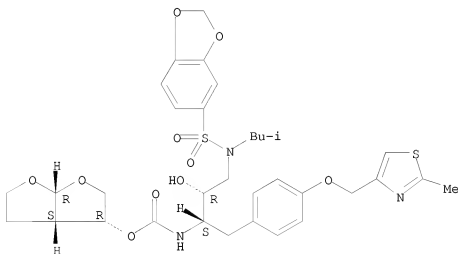
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(single-dose safety and pharmacokinetics of brexanavir, a novel human immunodeficiency virus protease inhibitor)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:456993 HCAPLUS

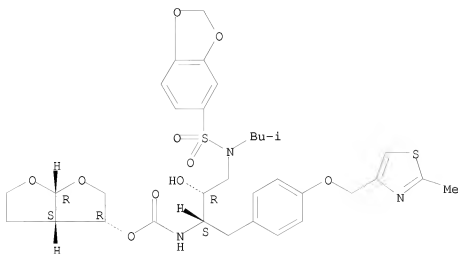
DOCUMENT NUMBER: 144:474844

TITLE: Conjugates with enhanced cell uptake activity

INVENTOR(S): Bonny, Christophe; Coquoz, Didier; Chen, Jianhua
 PATENT ASSIGNEE(S): Xigen S.A., Switz.
 SOURCE: Eur. Pat. Appl., 65 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1656951	A1	20060517	EP 2004-26934	20041112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
AU 2005303949	A1	20060518	AU 2005-303949	20051109
CA 2585421	A1	20060518	CA 2005-2585421	20051109
WO 2006050930	A2	20060518	WO 2005-EP11991	20051109
WO 2006050930	A3	20070426		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA				
EP 1809334	A2	20070725	EP 2005-811041	20051109
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
CN 101072589	A	20071114	CN 2005-80038728	20051109
PRIORITY APPLN. INFO.:			EP 2004-26934	A 20041112
			WO 2005-EP11991	W 20051109
AB	This invention relates to a conjugate mol. comprising at least one first portion (I) comprising a carrier sequence and at least one second portion (II) comprising at least one anti-tumor drug mol. or a protease inhibitor mol., said conjugate mol. comprising D-enantiomeric amino acids in its portion (I). Furthermore, the invention relates to pharmaceutical compns. containing said conjugate mol. as well as to the use of said conjugate mol. for therapeutical treatment. Methods for improving cell permeability are disclosed as well.			
IT	313682-08-5, Proteinase Inhibitor 640385 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (Vertex 385; D-enantiomeric peptide conjugates with enhanced cell uptake activity)			
RN	313682-08-5 HCAPLUS			
CN	Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)-(2-methylpropyl)amino]-2-hydroxy-1-[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)			

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:367270 HCAPLUS
 DOCUMENT NUMBER: 144:398367
 TITLE: Amorphous pharmaceutical compositions comprising rosiglitazone
 INVENTOR(S): Ignatious, Francis; Sun, Linghong; Craig, Andrew; Crowe, David; Ho, Tim; Millan, Michael
 PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
 SOURCE: U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 523,835.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006083784	A1	20060420	US 2005-64890	20050224
WO 2004014304	A2	20040219	WO 2003-US24641	20030807
WO 2004014304	A3	20040624		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2006013869	A1	20060119	US 2005-523835	20050207

WO 2006090150 A1 20060831 WO 2006-GB632 20060223
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
EP 1853262 A1 20071114 EP 2006-709864 20060223
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR
IN 2007DN06569 A 20070921 IN 2007-DN6569 20070824
KR 2007112217 A 20071122 KR 2007-721885 20070921
PRIORITY APPLN. INFO.:
US 2002-401726P P 20020807
WO 2003-US24641 W 20030807
US 2005-523835 A2 20050207
US 2005-64890 A 20050224
WO 2006-GB632 W 20060223
AB The present invention is directed to use of electrospinning, i.e. the process of making polymer nanofibers from either a solution or melt under elec. forces, to prepare stable, solid dispersions of amorphous drugs in polymer nanofibers. The present invention is also directed to the process of making solid dispersions of amorphous forms and compns. of rosiglitazone and its pharmaceutically acceptable salts. A 3.1 weight% solution of rosiglitazone mesylate 2-PrOH-water was spray dried to give an amorphous powder.
IT 313682-08-5
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous pharmaceutical compns. comprising rosiglitazone)
RN 313682-08-5 HCAPLUS
CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.

OTHER SOURCE(S):

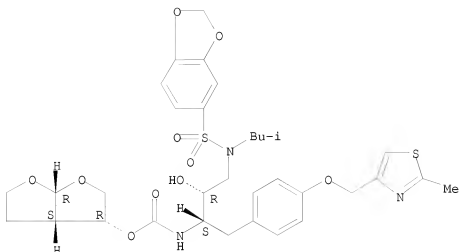
MARPAT 144:370090

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

- AB The invention relates to compds. of general formula I, which demonstrate protective effects on target cells from HIV infection in a manner as to bind specifically to the chemokine receptor, and which affect the binding of the natural ligand or chemokine to a receptor such as CXCR4 and/or CCR5 of a target cell. In compds. I, p is 0-2; each R1 is independently selected from halo, alkyl, haloalkyl, alkenyl, cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl, etc.; n is 0-2; each R2 is independently selected from H, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, etc.; R3 is selected from H, halo, alkyl, haloalkyl, cycloalkyl, alkenyl, alkynyl, etc.; each R4 is independently selected from halo, cyano, nitro, alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl, etc.; m is 0-2; Y is (un)substituted alkylene, (un)substituted cycloalkylene, alkenylene, cycloalkenylene, or alkynylene; and Z is (un)substituted amino, (un)substituted aminoaryl, (un)substituted heteroaryl, (un)substituted heterocyclyl, etc.; including pharmaceutically acceptable salts and esters thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier, optionally containing one or more addnl. therapeutic agents, as well as to the use of the compns. for the prevention of infection of a cell by HIV. Reductive amination of quinolinone II with tert-Bu N-(4-aminobutyl)carbamate and reductive amination with 5-fluoroimidazo[1,2-a]pyridine-2-carboxaldehyde gave amine III, which underwent substitution with tert-Bu piperazine-1-carboxylate and deprotection to give aminotetrahydroquinoline IV. Several compds. of the invention show HIV anti-infective activity, e.g., compound IV expresses activity of 2.2 nM in an HOS HIV-1 anti-infectivity assay.
- IT 313682-08-5, Brecanavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of aminotetrahydroquinolines as cytoprotectants from HIV infection)
- RN 313682-08-5 HCAPLUS
- CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:270625 HCAPLUS

DOCUMENT NUMBER: 144:266487

TITLE: Discovery of next generation inhibitors of HIV protease

AUTHOR(S): Spaltenstein, Andrew; Kazmierski, Wieslaw M.; Miller, John F.; Samano, Vicente

CORPORATE SOURCE: Division of Chemistry, MV CEDD, GlaxoSmithKline, Research Triangle Park, NC, 27709, USA

SOURCE: Current Topics in Medicinal Chemistry (Sharjah, United Arab Emirates) (2005), 5(16), 1589-1607

CODEN: CTMCCL; ISSN: 1568-0266

PUBLISHER: Bentham Science Publishers Ltd.

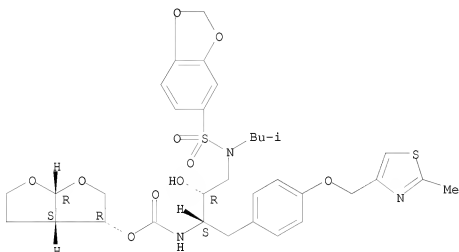
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Due to factors such as resistance and long-term side effects as well as dosing regimen-related adherence issues, HIV therapy is a constantly moving target. HIV-1 protease inhibitors had an immediate and dramatic impact on the outcome of HIV/AIDS when launched in late 1995, and the search for new and improved next generation mols. has been under way in many labs. At GlaxoSmithKline (GSK) and Vertex Pharmaceuticals, this effort focused on 2 key issues, patient compliance and viral resistance. Using a water-solubilizing prodrug approach, the pill burden in delivering a protease inhibitor, Amprenavir, was dramatically decreased. By eliminating the large amts. of excipients necessary for the original soft-gel formulation, Fosamprenavir (Lexiva/Telzir) delivers the clin. efficacious dose of Amprenavir with 2 compact tablets per dose, compared to 8 gel capsules. The efforts to overcome viral resistance to 1st generation protease inhibitors by further elaborating the SAR of the Amprenavir and related scaffolds led to successive and dramatic improvements in wild-type antiviral potencies, and ultimately to the discovery of ultra-potent mols. with very favorable overall resistance profiles. The selection of GW640385 (Brecanavir - USAN approved only) as a clin. candidate and its progression into current phase 2 dose ranging studies represents the culmination of the effort toward the next

generation protease inhibitors.
 IT 313682-08-5, Brecanavir
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (discovery of next generation inhibitors of HIV protease)
 RN 313682-08-5 HCAPLUS
 CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl][methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.

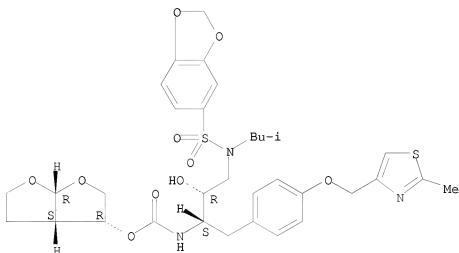


REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:252581 HCAPLUS
 DOCUMENT NUMBER: 144:425067
 TITLE: In vitro development of resistance to human immunodeficiency virus protease inhibitor GW640385
 AUTHOR(S): Yates, P. J.; Hazen, R.; St. Clair, M.; Boone, L.; Tisdale, M.; Elston, R. C.
 CORPORATE SOURCE: GlaxoSmithKline Inc., Stevenage, UK
 SOURCE: Antimicrobial Agents and Chemotherapy (2006), 50(3), 1092-1095
 CODEN: AMACQ; ISSN: 0066-4804
 PUBLISHER: American Society for Microbiology
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Development of in vitro resistance to GW640385, a new human immunodeficiency virus type 1 protease inhibitor, was studied. Variants characterized included one with <4-fold resistance and amino acid substitutions Q58E/A71V (protease) and P452K (Gag) and one with >50-fold resistance and amino acid substitutions L10F/G16E/E21K/A28S/M46I/F53L/A71V (protease) and L449F/P453T (Gag). The A28S substitution substantially reduced replication capacity.

IT 313682-08-5
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (in vitro development of resistance to human immunodeficiency virus
 protease inhibitor GW640385)
 RN 313682-08-5 HCAPLUS
 CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-
 methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-
 thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-
 b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:188865 HCAPLUS
 DOCUMENT NUMBER: 144:432712
 TITLE: Ultra-potent P1 modified arylsulfonamide HIV protease inhibitors: The discovery of GW0385
 AUTHOR(S): Miller, John F.; Andrews, C. Webster; Brieger, Michael; Furfine, Eric S.; Hale, Michael R.; Hanlon, Mary H.; Hazen, Richard J.; Kaldor, Istvan; McLean, Ed W.; Reynolds, David; Sammond, Douglas M.; Spaltenstein, Andrew; Tung, Roger; Turner, Elizabeth M.; Xu, Robert X.; Sherrill, Ronald G.
 CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(7), 1788-1794
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 144:432712
 AB A novel series of P1 modified HIV protease inhibitors was synthesized and evaluated for in vitro antiviral activity against wild-type virus and

protease inhibitor-resistant viruses. Optimization of the P1 moiety resulted in compds. with femtomolar enzyme activities and cellular antiviral activities in the low nanomolar range culminating in the identification of clin. candidate GW0385.

IT 313682-08-5P, GW0385

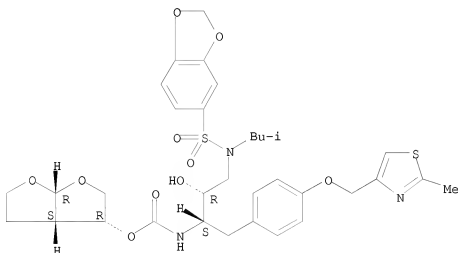
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of the dioxabicyclooctyl thiazolylmethoxybenzyl-substituted (benzodioxolylsulfonylamino)propylcarbamate GW0385 as an anti-HIV agent and its pharmacokinetics and behavior in resistant HIV strains)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 28 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:698347 HCAPLUS

DOCUMENT NUMBER: 143:194248

TITLE: Therapeutic combinations containing an amino acid

INVENTOR(S): Hammond, Jennifer Lou; Patick, Amy Karen

PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 25 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

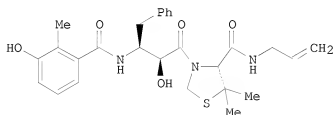
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US	2005171038	A1	20050804	US	2005-46260	20050128
AU	2005216710	A1	20050909	AU	2005-216710	20050117
CA	2555171	A1	20050909	CA	2005-2555171	20050117
WO	2005082362	A1	20050909	WO	2005-IB101	20050117
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP	1713470	A1	20061025	EP	2005-702264	20050117
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS					
BR	2005006493	A	20070213	BR	2005-6493	20050117
CN	1938017	A	20070328	CN	2005-80010030	20050117
JP	2007519704	T	20070719	JP	2006-550331	20050117
NO	2006003483	A	20060830	NO	2006-3483	20060731
MX	2006PA08632	A	20060904	MX	2006-PA8632	20060731
IN	2006DN04522	A	20070824	IN	2006-DN4522	20060804
PRIORITY APPLN. INFO.:				US	2004-540749P	P 20040130
				US	2004-615000P	P 20041001
				WO	2005-IB101	W 20050117

OTHER SOURCE(S): CASREACT 143:194248

GI



I

AB The invention is related to methods for treating an HIV infection by using a therapeutically effective amount of a combination of compds., including I and its related N-amide derivs. The invention is also related to compns. comprising certain compds. useful as inhibitors of the HIV protease enzyme and at least one addnl. therapeutic agent. In an XTT dye reduction method, I in combination with ritonavir acted synergistically against HIV-1 infection.

IT 313682-08-5, VX 385

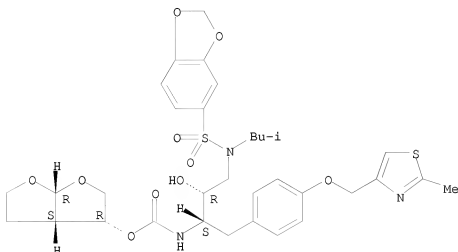
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy agent; compns. comprising an amino acid amide HIV protease inhibitor)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)-(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-

thiazolyl)methoxy]phenyl)methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:74120 HCAPLUS

DOCUMENT NUMBER: 142:176697

TITLE: Preparation of spiro compounds for the modulation of chemokine receptor activity

INVENTOR(S): Chan, Chun Kong; Zhang, Ming-Qiang; Moinet, Christophe; Proulx, Melanie; Reddy, Thumkunta Jagadeeswar; Courchesne, Marc

PATENT ASSIGNEE(S): Virochem Pharma Inc., Can.

SOURCE: PCT Int. Appl., 338 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

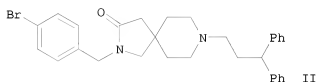
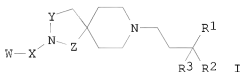
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

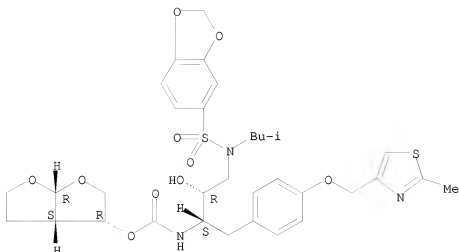
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005007656	A1	20050127	WO 2004-CA1048	20040716
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2573951	A1	20050127	CA 2004-2573951	20040716

EP 1776362 A1 20070425 EP 2004-761573 20040716
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, HR, LT, LV, MK
 US 2005075326 A1 20050407 US 2004-893583 20040719
 PRIORITY APPLN. INFO.: US 2003-487973P P 20030718
 WO 2004-CA1048 W 20040716
 OTHER SOURCE(S): MARPAT 142:176697
 GI



- AB The title compds. I [Y, Z and X = CH₂, CO, CR₄R₅; W = H, alkyl, alkenyl, aryl, etc.; R₁ = H, OH, alkyl, etc.; R₂ = alkyl, alkenyl, alkynyl, aryl, heterocyclyl; R₃ = H, alkyl, alkenyl, alkynyl, aryl; R₄, R₅ = H, alkyl, alkenyl, alkynyl, aryl] and their pharmaceutically acceptable salts, useful for the modulation of CCR5 chemokine receptor activity and the treatment or prevention of diseases associated therewith, were prepared E.g., a multi-step synthesis of II.HCl, starting from tert-Bu 1-oxo-2,8-diaza-spiro[4.5]decane-8-carboxylate and 4-bromobenzyl bromide, was given. The compds. I have been found to have activity in binding to the CCR5 receptor, generally with an IC₅₀ values of < 25 μM. Certain compds. I have also been tested in an assay for HIV activity, and generally having an IC₅₀ values of < 1 μM.
- IT 313682-08-5, VX 385
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (co-drug; preparation of spiro compds. for treating diseases associated with CCR5 chemokine receptor activity in combination with other agents)
- RN 313682-08-5 HCAPLUS
- CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)-(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 30 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:14172 HCAPLUS

DOCUMENT NUMBER: 142:114047

TITLE: A preparation of furofuranyl derivative, useful as inhibitor of HIV aspartyl protease

INVENTOR(S): Roberts, John Charles; Toczko, Jennifer Fell

PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; Martin, Michael Tolar

SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000249	A2	20050106	WO 2004-US20353	20040625
WO 2005000249	A3	20050407		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1638960	A2	20060329	EP 2004-777060	20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				

JP 2007521277	T	20070802	JP 2006-517643	20040625
US 2006148865	A1	20060706	US 2005-560500	20051212
PRIORITY APPLN. INFO.:			US 2003-483002P	P 20030627
			WO 2004-US20353	W 20040625

OTHER SOURCE(S): CASREACT 142:114047
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

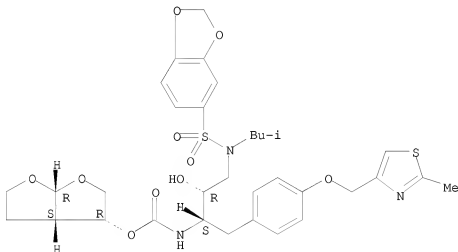
AB The invention relates to a preparation of furofuranyl derivative I, useful as inhibitor of HIV aspartyl protease (no biol. data). For instance, I was prepared via deprotection of II and coupling with III with a yield of 90% (example 2).

IT 313682-08-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:885959 HCAPLUS
DOCUMENT NUMBER: 142:51214
TITLE: Inhibition of Wild-Type and Mutant Human
Immunodeficiency Virus Type 1 Proteases by GW0385 and
Other Arylsulfonamides
AUTHOR(S): Hanlon, Mary H.; Porter, David J. T.; Furfine, Eric

S.; Spaltenstein, Andrew; Carter, H. Luke; Danger, Dana; Shu, Arthur Y. L.; Kaldor, Istvan W.; Miller, John F.; Samano, Vicente A.

CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, PA, 19405, USA

SOURCE: Biochemistry (2004), 43(45), 14500-14507

CODEN: BICHAJ; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The arylsulfonamide derivs. described herein were such potent inhibitors of human immunodeficiency virus type 1 (HIV-1) protease (enzyme, E) that values for the inhibition consts. (K_i) could not be determined by conventional steady-state kinetic techniques (i.e., the minimal enzyme concentration usable for the activity assay was much greater than the value of the dissociation constant). Consequently, two alternative methods were developed for estimation of K_i values. The first method employed kinetic detns. of values for k_1 and k_{-1} , from which K_i was determined (k_{-1}/k_1). The second method was a competitive displacement assay used to determine binding affinities of other inhibitors relative to that of GW0385. In these assays, the inhibitor of unknown affinity was used to displace $[3H]GW0385$ from $E \cdot [3H]GW0385$. From the concentration of $E \cdot [3H]GW0385$ at equilibrium, the concns. of enzyme-bound and free inhibitors were calculated, and the ratio of the K_i value of the unknown to that of GW0385 was determined ($K_i, \text{unknown}/K_i, \text{GW0385}$). The values of k_1 were calculated from data in which changes in the intrinsic protein fluorescence of the enzyme associated with inhibitor binding were directly or indirectly monitored. In the case of saquinavir, the fluorescence changes associated with complex formation were large enough to monitor directly. The value of k_1 for saquinavir was $62 \pm 2 \mu\text{M}^{-1} \text{ s}^{-1}$. In the case of GW0385, the fluorescence changes associated with complex formation were too small to monitor directly. Consequently, the value of k_1 was estimated from a competition experiment in which the effect of GW0385 on the

binding of E to saquinavir was determined. The value of k_1 for GW0385 was estimated from these expts. to be $137 \pm 4 \mu\text{M}^{-1} \text{ s}^{-1}$. Because $E \cdot [3H]GW0385$ was stable in the standard buffer at room temperature for greater than 33 days, the

value of the first-order rate constant for dissociation of $E \cdot [3H]GW0385$ (k_{-1}) could be estimated from the time-course for exchange of $E \cdot [3H]GW0385$ with excess unlabeled GW0385. The value of k_{-1} calculated from these data was $(2.1 \pm 0.1) \times 10^{-6} \text{ s}^{-1}$ ($t_{1/2} = 91 \text{ h}$). The K_i value of wild-type HIV-1 protease for GW0385, calculated from these values for k_1 and k_{-1} , was $15 \pm 1 \text{ nM}$. Three multidrug resistant enzymes had K_i values for GW0385 that were less than 5 pM .

IT 810687-57-1P

RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

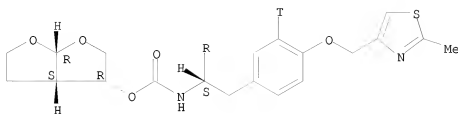
(inhibition of wild-type and drug-resistant mutant human immunodeficiency virus type 1 proteases by GW0385 and other arylsulfonamides monitored by fluorescence)

RN 810687-57-1 HCAPLUS

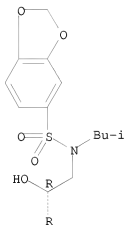
CN Carbamic acid, [(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]-3-t[methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

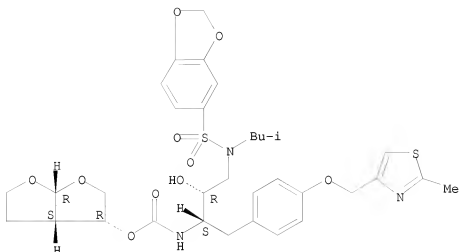


PAGE 2-A



- IT 313682-08-5, GW 0385
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 BIOL (Biological study)
 (inhibition of wild-type and drug-resistant mutant human
 immunodeficiency virus type 1 proteases by GW0385 and other
 arylsulfonamides monitored by fluorescence)
- RN 313682-08-5 HCAPLUS
- CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-
 methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-
 thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-
 b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.

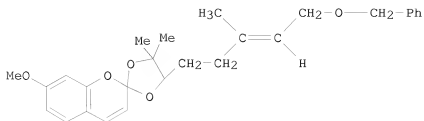


REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:252197 HCAPLUS
 DOCUMENT NUMBER: 140:281350
 TITLE: Spiro compounds for inhibiting the first-pass effect
 INVENTOR(S): Harris, James W.
 PATENT ASSIGNEE(S): Bioavailability System, LLC, USA
 SOURCE: U.S. Pat. Appl. Publ., 133 pp., Cont.-in-part of U.S.
 Ser. No. 793,416.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 5
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004058982	A1	20040325	US 2003-422848	20030425
US 6248776	B1	20010619	US 1999-251467	19990217
US 6476066	B1	20021105	US 2001-793416	20010227
US 2005214366	A1	20050929	US 2005-81024	20050316
US 7230027	B2	20070612		
US 2007244188	A1	20071018	US 2007-696198	20070404
PRIORITY APPLN. INFO.:			US 1999-251467	A3 19990217
			US 2001-793416	A2 20010227
			US 1997-56382P	P 19970826
			US 1997-997259	A2 19971223
			US 2003-422848	B1 20030425
			US 2005-81024	A1 20050316

OTHER SOURCE(S): MARPAT 140:281350
 GI



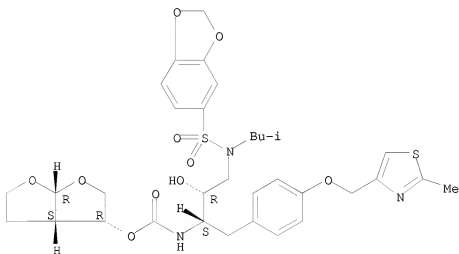
AB Compns., methods, etc. for addressing the first-pass effect are presented. An example compound prepared was I. Also processing citrus oils to obtain the compds. is given as examples as well as assessment of human cytochrome P 450-mediated biotransformation.

IT 313682-08-5, VX 385
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spiro compds. for inhibiting the first-pass effect)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2008 ACS on SIN

ACCESSION NUMBER: 2004:142902 HCAPLUS

DOCUMENT NUMBER: 140:187404

TITLE: Electrospun amorphous pharmaceutical compositions

INVENTOR(S): Ignatious, Francis; Sun, Linghong

PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA

SOURCE: PCT Int. Appl., 36 pp.

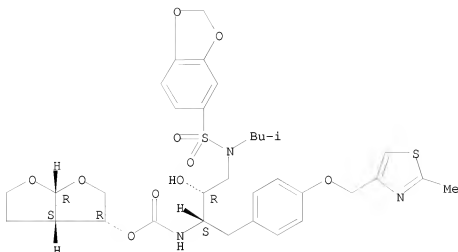
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014304	A2	20040219	WO 2003-US24641	20030807
WO 2004014304	A3	20040624		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2494865	A1	20040219	CA 2003-2494865	20030807
AU 2003258120	A1	20040225	AU 2003-258120	20030807
EP 1534250	A2	20050601	EP 2003-784959	20030807
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003013222	A	20050614	BR 2003-13222	20030807
CN 1684673	A	20051019	CN 2003-823237	20030807
JP 2005534716	T	20051117	JP 2004-527797	20030807
ZA 2005000563	A	20060726	ZA 2005-563	20050120
MX 2005PA01499	A	20050419	MX 2005-PA1499	20050207
US 2006013869	A1	20060119	US 2005-523835	20050207
US 2006083784	A1	20060420	US 2005-64890	20050224
NO 2005001123	A	20050506	NO 2005-1123	20050302
PRIORITY APPLN. INFO.:			US 2002-401726P	P 20020807
			WO 2003-US24641	W 20030807
			US 2005-523835	A2 20050207
AB	The present invention is directed to use of electrospinning, i.e. the process of making polymer nanofibers from either a solution or melt under elec. forces, to prepare stable, solid dispersions of amorphous drugs in polymer nanofibers. Thus, carvedilol-HBr monohydrate was dissolved in THF and water. The solution was added to Polyox WSR1105 in MeCN solution. This solution was spun to give nanofibers, and the morphol. of the drug was shown to be amorphous.			
IT	313682-08-5			
RL:	PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)			
	(electrospun amorphous pharmaceutical compns.)			
RN	313682-08-5 HCAPLUS			
CN	Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)-(2-methylpropyl)amino]-2-hydroxy-1-[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)			

Absolute stereochemistry.



L14 ANSWER 34 OF 34 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:900607 HCAPLUS

DOCUMENT NUMBER: 134:56676

TITLE: Preparation of arylsulfonamides as inhibitors of aspartyl protease

INVENTOR(S): Hale, Michael Robin; Tung, Roger; Price, Stephen; Wilkes, Robin David; Schairer, Wayne Carl; Jarvis, Ashley Nicholas; Spaltenstein, Andrew; Furfine, Eric Steven; Samano, Vicente; Kaldor, Istvan; Miller, John Franklin; Brieger, Michael Stephen

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Inc., USA; et al.

SOURCE: PCI Int. Appl., 396 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

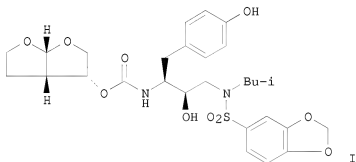
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000076961	A1	20001221	WO 2000-US15781	20000608
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2380858	A1	20001221	CA 2000-2380858	20000608
BR 2000011745	A	20020319	BR 2000-11745	20000608
EP 1194404	A1	20020410	EP 2000-941279	20000608
EP 1194404	B1	20060503		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			

IE, SI, LT, LV, FI, RO, CY				
TR 200200407	T2	20020821	TR 2002-407	20000608
JP 2003502309	T	20030121	JP 2001-503821	20000608
TR 200202528	T2	20030221	TR 2002-2528	20000608
HU 2003000385	A2	20030728	HU 2003-385	20000608
HU 2003000385	A3	20070529		
NZ 516003	A	20040227	NZ 2000-516003	20000608
TW 593248	B	20040621	TW 2000-89111145	20000608
AU 779994	B2	20050224	AU 2000-56006	20000608
IN 2000CA00336	A	20050311	IN 2000-CA336	20000608
AT 325091	T	20060615	AT 2000-941279	20000608
EP 1686113	A1	20060802	EP 2006-9072	20000608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PT 1194404	T	20060831	PT 2000-941279	20000608
ES 2263478	T3	20061216	ES 2000-941279	20000608
TR 200603871	T2	20070122	TR 2006-3871	20000608
US 6878728	B1	20050412	US 2000-591464	20000609
IN 2001KN01289	A	20050311	IN 2001-KN1289	20011206
NO 2001006034	A	20020118	NO 2001-6034	20011210
NO 323951	B1	20070723		
MX 2001PA12808	A	20020722	MX 2001-PA12808	20011211
ZA 2001010177	A	20030113	ZA 2001-10177	20011211
KR 762188	B1	20071004	KR 2001-716293	20011211
HK 1046899	A1	20070302	HK 2002-106939	20020923
US 2004122000	A1	20040624	US 2003-691333	20031021
IN 2007KN00501	A	20070706	IN 2007-KN501	20070209
PRIORITY APPLN. INFO.:				
			US 1999-139070P	P 19990611
			US 2000-190211P	P 20000317
			EP 2000-941279	A3 20000608
			WO 2000-US15781	W 20000608
			US 2000-591464	A3 20000609
			IN 2001-KN1289	A3 20011206

OTHER SOURCE(S): MARPAT 134:56676
GI



AB The title arylsulfonamides, namely (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 3-aryl-sulfonylamino-1-(4-hydroxyphenyl)-2-hydroxypropylcarbamate derivs. (e.g. I) are prepared. These compds. are particularly well suited for inhibiting HIV-1 and HIV-2 protease activity and consequently, may be advantageously used as anti-viral agents against the HIV-1 and HIV-2 viruses. They are useful for treating with a patient diagnosed with AIDS,

AIDS related complex (ARC), progressive generalized lymphadenopathy (PGL), Kaposi's sarcoma, thrombocytopenic purpura, or AIDS-related neuropathic conditions such as AIDS dementia complex, multiple sclerosis or tropical paraperesis, etc. Thus, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 3-[N-(1,3-benzodioxol-5-ylsulfonyl)-N-isobutylamino]-1-(4-hydroxyphenyl)-2-hydroxypropylcarbamate underwent Mitsunobu reaction with phenethyl alc. using Ph3P and di-tert-Bu azodicarbonate in CH2Cl2 at room temperature for 1.5

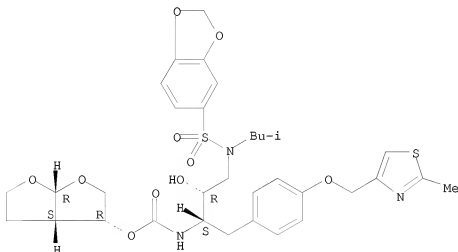
h to give 72% I. I showed IC50 of <0.001, <0.001, and 0.01-0.001 μ M against drug-resistant HIV strains, i.e. wild type, mutant HIV-1 EP13, and mutant D545701-14 HIV strains, resp., in MT-4 cells.

IT 313682-08-5P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of arylsulfonamides as inhibitors of HIV aspartyl protease and antiviral agents)

RN 313682-08-5 HCAPLUS

CN Carbamic acid, N-[(1S,2R)-3-[(1,3-benzodioxol-5-ylsulfonyl)-(2-methylpropyl)amino]-2-hydroxy-1-[[4-[(2-methyl-4-thiazolyl)methoxy]phenyl]methyl]propyl]-, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
332.31	573.89

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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CA SUBSCRIBER PRICE

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PASSWORD:

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	332.31	573.89
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
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CA SUBSCRIBER PRICE	-47.20	-47.20

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
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FULL ESTIMATED COST	332.31	573.89
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-47.20	-47.20

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DICTIONARY FILE UPDATES: 4 FEB 2008 HIGHEST RN 1001463-85-9

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<http://www.cas.org/support/stngen/stdoc/properties.html>

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ring nodes :
1 2 3 4 5 6 7 8
chain bonds :
4-9 9-10
ring bonds :
1-2 1-5 2-3 2-6 3-4 3-8 4-5 6-7 7-8
exact/norm bonds :
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exact bonds :
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Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS

L16 STRUCTURE UPLOADED

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FULL SEARCH INITIATED 16:13:51 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 15 TO ITERATE

100.0% PROCESSED 15 ITERATIONS

7 ANSWERS

SEARCH TIME: 00.00.01

L17 7 SEA EXA FUL L16

=> file hcaplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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634.20

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

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FILE COVERS 1907 - 5 Feb 2008 VOL 148 ISS 6
FILE LAST UPDATED: 4 Feb 2008 (20080204/ED)

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(FILE 'HOME' ENTERED AT 15:49:32 ON 05 FEB 2008)

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L3	STRUCTURE UPLOADED
L4	STRUCTURE UPLOADED
L5	0 L1 EXA
L6	2 L1 EXA FULL
L7	8 L2 EXA FULL
L8	1 L3 EXA FULL
L9	1 L4 EXA FUL

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L10	1 L6 AND L7
L11	1 L6 AND L8
L12	1 L6 AND L9
L13	1 L10 AND L11 AND L12
L14	34 L6
L15	24 L7

FILE 'REGISTRY' ENTERED AT 16:13:38 ON 05 FEB 2008

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FILE 'HCAPLUS' ENTERED AT 16:13:56 ON 05 FEB 2008

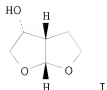
=> 117 and 17

	41 L17
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L18	12 L17 AND L7

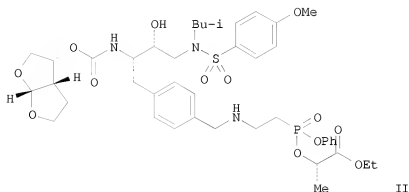
=> d ibib abs hitstr 1-12

L18 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2007:1275513 HCAPLUS
 DOCUMENT NUMBER: 147:502340
 TITLE: Process for preparation of carbamic acid bisfuranyl esters as HIV protease inhibitors and their use in the treatment of retroviral infection
 INVENTOR(S): Crawford, Kenneth R.; Dowdy, Eric D.; Gutierrez, Arnold; Polniaszek, Richard P.; Yu, Richard Hung Chiu
 PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
 SOURCE: PCT Int. Appl., 58pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007126812	A2	20071108	WO 2007-US7564	20070329
WO 2007126812	A3	20071221		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
US 2008004242	A1	20080103	US 2007-729522	20070329
PRIORITY APPLN. INFO.:			US 2006-787126P	P 20060329
OTHER SOURCE(S):	CASREACT 147:502340			
GI				



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II

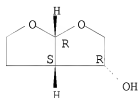
AB A process for the synthesis of bisfuran intermediates, e.g., I useful for preparing antiviral HIV protease inhibitor compds. is hereby disclosed. Example compound II was prepared as adipic acid salt and succinic acid salts, using intermediate I as the key component in the preparation. The invention compds. were evaluated for their HIV protease inhibitory activity (no data).

IT 156928-09-5P
 RL: BSU (Biological study, unclassified); IMF (Industrial manufacture);
 PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study);
 PREP (Preparation); RACT (Reactant or reagent)
 (preparation of carbamic acid bisfuranyl ester compds. as HIV protease inhibitors useful in treatment and prevention of retroviral infection)

RN 156928-09-5 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

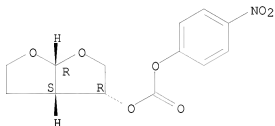
Absolute stereochemistry. Rotation (-).



IT 192725-55-6P
 RL: BSU (Biological study, unclassified); IMF (Industrial manufacture);
 RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP
 (Preparation); RACT (Reactant or reagent)
 (preparation of carbamic acid bisfuranyl ester compds. as HIV protease

inhibitors useful in treatment and prevention of retroviral infection)
 RN 192725-55-6 HCAPLUS
 CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L18 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1131417 HCAPLUS

DOCUMENT NUMBER: 148:33642

TITLE: Research and Development of an Efficient Synthesis of Hexahydrofuro[2,3-b]furan-3-ol Moiety-A Key Component of the HIV Protease Inhibitor Candidates

AUTHOR(S): Yu, Richard H.; Polniaszek, Richard P.; Becker, Mark W.; Cook, Charles M.; Yu, Lok Him L.

CORPORATE SOURCE: Process Research Department, Gilead Sciences, Inc., Foster City, CA, 94404, USA

SOURCE: Organic Process Research & Development (2007), 11(6), 972-980

CODEN: OPRDFK; ISSN: 1083-6160

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 148:33642

AB A highly efficient method for the synthesis of racemic hexahydrofuro[2,3-b]furan-3-ol has been developed utilizing a lanthanide catalyst, such as Yb(fod)3, to promote condensation of 2,3-dihydrofuran and glycolaldehyde dimer. Access to either optically enriched enantiomer of bisfuran alc. can be obtained by using this method employing chiral ligands with the lanthanide catalyst. This method has been demonstrated to be a robust and scalable process with potential application for the construction of a variety of furo[2,3-b]furan derivs.

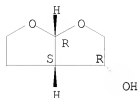
IT 156928-09-5P

RL: BPN (Biosynthetic preparation); IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent) (scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)

RN 156928-09-5 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



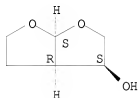
IT 162119-33-7P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)

RN 162119-33-7 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



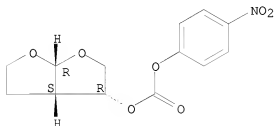
IT 192725-55-6P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



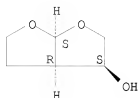
IT 156928-10-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(scalable synthesis of enantiopure hexahydrofuro[2,3-b]furan-3-ol as a key component of the HIV protease inhibitor candidates)

RN 156928-10-8 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:449362 HCAPLUS

DOCUMENT NUMBER: 145:8179

TITLE: Process for the preparation of pyrimidinyl aminodiphenylhexane derivatives as retroviral protease inhibiting prodrugs

INVENTOR(S): Kumar, Gondi N.; Herrin, Thomas R.; Kempf, Dale J.; Betebenner, David A.; Chen, Xiaoqi; Norbeck, Daniel W.; Sham, Hing Leung; Patel, Ketan M.; Liu, Jih-Hua; Tien, Jieh-Heh J.; Stoner, Eric J.; Stengel, Peter J.; Plata, Daniel J.; Oliver, Patricia A.; Kolaczowski, Lawrence; Hannick, Steven M.; Dickman, Daniel A.; Cooper, Arthur J.; Condon, Stephen L.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: Aust. Pat. Appl., 252 pp.

CODEN: AUXXCM

DOCUMENT TYPE: Patent

LANGUAGE: English

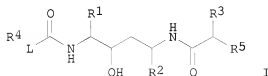
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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AU 2004201149	A1	20040422	AU 2004-201149	20040318
AU 2004201149	B2	20070802		
AU 2007231810	A1	20071129	AU 2007-231810	20071101
PRIORITY APPLN. INFO.:			AU 2001-13690	A3 20010112
			AU 2004-201149	A3 20040318

OTHER SOURCE(S): MARPAT 145:8179

GI



AB Pyrimidinyl aminodiphenylhexane derivs. I, wherein R1 and R2 are independently lower alkyl, cycloalkyl-alkyl, aryl-alkyl; R3 is lower

alkyl, cycloalkyl-alkyl, hydroxy-alkyl; R4 is aryl, heterocyclic; R5 is five- or six-membered heterocycle containing at least one nitrogen atom; L is O, S, NH, N-alkyl, , N-cycloalkyl, N-cycloalkyl-alkyl, O-alkylenyl, SO-alkylenyl, S(O)2-alkylenyl, alkylenyl-O, alkylenyl-S, alkylenyl, alkenylenyl, were prepared and tested in vitro and in human as retroviral protease inhibiting prodrugs. Thus, (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-[2S-(1-tetrahydropyrimidin-2-onyl)-3-methylbutanoyl]amino-1,6-diphenylhexane was prepared via coupling of (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-amino-1,6-diphenylhexane with 2S-(1-tetrahydro-pyrimidin-2-onyl)-3-methylbutanoic acid. The present invention relates to novel compds. and a composition and method for inhibiting retroviral proteases and in particular for inhibiting human immunodeficiency virus (HIV) protease, a composition and method for inhibiting a retroviral infection and in particular an HIV infection, processes for making the compds. and synthetic intermediates employed in the processes. While the compound of the invention can be administered as the sole active pharmaceutical agent, it can also be used in combination with one or more immunomodulators, antiviral agents, other antiinfective agents, or vaccines. The compds. of the invention are useful for inhibiting retroviral protease, in particular HIV protease, in vitro or in vivo (especially in mammals and in particular in humans). Total daily dose administered to a human or other mammal host in single or divided doses may be in ams., for example, from 0.001 to 300 mg/kg body weight daily and more usually 0.1 to 20 mg/kg body weight daily.

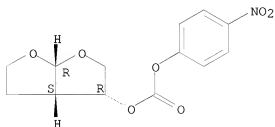
IT 192725-55-6P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation of pyrimidinyl aminodiphenylhexane derivs. as retroviral protease inhibiting prodrugs)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



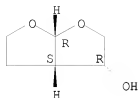
IT 156928-09-5

RL: RCT (Reactant); RACT (Reactant or reagent)
(process for preparation of pyrimidinyl aminodiphenylhexane derivs. as retroviral protease inhibiting prodrugs)

RN 156928-09-5 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L18 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:589326 HCAPLUS

DOCUMENT NUMBER: 143:267225

TITLE: Novel P1 chain-extended HIV protease inhibitors possessing potent anti-HIV activity and remarkable inverse antiviral resistance profiles

AUTHOR(S): Miller, John F.; Brieger, Michael; Furfine, Eric S.; Hazen, Richard J.; Kaldor, Istvan; Reynolds, David; Sherrill, Ronald G.; Spaltenstein, Andrew

CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA

SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(15), 3496-3500

CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 143:267225

AB A novel series of tyrosine-derived HIV protease inhibitors was synthesized and evaluated for in vitro antiviral activity against wild-type virus and two protease inhibitor-resistant viruses. All of the compds. had wild-type antiviral activities that were similar to or greater than several currently marketed HIV protease inhibitors. In addition, a number of compds. in this series were more potent against the drug-resistant mutant viruses than they were against wild-type virus.

IT 156928-09-5

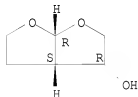
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of P1 chain-extended HIV protease inhibitors possessing potent anti-HIV activity and remarkable inverse antiviral resistance profiles)

RN 156928-09-5 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 192725-55-6P

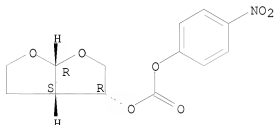
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of P1 chain-extended HIV protease inhibitors possessing potent anti-HIV activity and remarkable inverse antiviral resistance profiles)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:588404 HCAPLUS

DOCUMENT NUMBER: 143:133693

TITLE: Preparation of amino acid derivatives as HIV protease inhibitors

INVENTOR(S): Degoe, David A.; Flentge, Charles A.; Flosi, William J.; Grampovnik, David J.; Kempf, Dale J.; Klein, Larry L.; Yeung, Ming C.; Randolph, John T.; Wang, Xiu C.; Yu, Su

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 279 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005148623	A1	20050707	US 2004-8713	20041209
PRIORITY APPLN. INFO.:			US 2003-528974P	P 20031211

OTHER SOURCE(S): MARPAT 143:133693

AB The invention relates to amino acid derivs. A-NHCHR6CHR5CHR4CHR3NHCOCHR2NHCO2R1 [A is an amino acid or acyl residue of defined structure; R1, R2, R3, R6 are independently (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl or heteroaryl; R4, R5 are H (not both), OH or substituted hydroxyl], including pharmaceutically-acceptable salts, prodrugs or stereoisomers, having HIV protease inhibitory activity. Thus, Me (1S,4R,6S,7S,10S)-7-benzyl-1,10-di-tert-butyl-6-hydroxy-2,9,12-trioxo-4-[4-(2-pyridinyl)benzyl]-13-oxa-3,8,11-triazatetradec-1-ylcarbamate was prepared by a multistep procedure, which includes the reaction of intermediate tert-Bu (1S,2S,4R)-4-amino-1-benzyl-2-hydroxy-5-[4-(2-pyridinyl)phenyl]pentylcarbamate with N-protected L-tert-leucine. Comps. of the invention showed EC50 values in the range 0.7 nM to >3.2 μM

against wild-type HIV.

IT 192725-55-6P

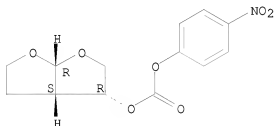
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amino acid derivs. as HIV protease inhibitors)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 162119-33-7

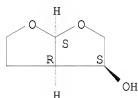
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of amino acid derivs. as HIV protease inhibitors)

RN 162119-33-7 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



L18 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:527398 HCAPLUS

DOCUMENT NUMBER: 143:78485

TITLE: Preparation of amino acid derivatives as HIV protease inhibitors

INVENTOR(S): DeGoey, David A.; Flentge, Charles A.; Flosi, William J.; Grampovnik, David J.; Kempf, Dale J.; Klein, Larry L.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 204 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

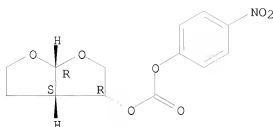
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005131017	A1	20050616	US 2003-733946	20031211
CA 2549098	A1	20050630	CA 2004-2549098	20041209
WO 2005058841	A2	20050630	WO 2004-US41658	20041209
WO 2005058841	A3	20060309		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1697344	A2	20060906	EP 2004-813910	20041209
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU			
JP 2007516260	T	20070621	JP 2006-544070	20041209
MX 2006PA06612	A	20060831	MX 2006-PA6612	20060609
PRIORITY APPLN. INFO.:			US 2003-733946	A 20031211
			WO 2004-US41658	W 20041209
OTHER SOURCE(S):	CASREACT 143:78485; MARPAT 143:78485			
AB	The invention relates to amino acid derivs. A-NHCHR6CHR5CHR4CHR3NHCOCHR2NHCO2R1 [A is an amino acid or acyl residue of defined structure; R1, R2, R3, R6 are independently (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclyl, aryl or heteroaryl; R4, R5 are H (not both), OH or substituted hydroxyl], including pharmaceutically-acceptable salts, stereoisomers, esters or prodrugs, having HIV protease inhibitory activity. Thus, Me (1S,4R,6S,7S,10S)-7-benzyl-1,10-di-tert-butyl-6-hydroxy-2,9,12-trioxo-4-[4-(2-pyridinyl)benzyl]-13-oxa-3,8,11-triazatetradec-1-ylcarbamate was prepared by a multistep procedure, which includes the reaction of intermediate tert-Bu (1S,2S,4R)-4-amino-1-benzyl-2-hydroxy-5-[4-(2-pyridinyl)phenyl]pentylcarbamate with N-protected L-tert-leucine. Compds. of the invention showed EC50 values 0.7-300 nM against wild-type HIV.			
IT	192725-55-6P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of amino acid derivs. as HIV protease inhibitors)			
RN	192725-55-6 HCAPLUS			
CN	Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)			

Absolute stereochemistry. Rotation (-).



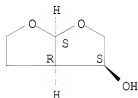
IT 162119-33-7

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of amino acid derivs. as HIV protease inhibitors)

RN 162119-33-7 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)-rel- (CA INDEX NAME)

Relative stereochemistry.



L18 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:14172 HCAPLUS

DOCUMENT NUMBER: 142:114047

TITLE: A preparation of furofuran derivative, useful as
inhibitor of HIV aspartyl protease

INVENTOR(S): Roberts, John Charles; Toczko, Jennifer Fell

PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA; Martin, Michael
Tolar

SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000249	A2	20050106	WO 2004-US20353	20040625
WO 2005000249	A3	20050407		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RM: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG

EP 1638960 A2 20060329 EP 2004-777060 20040625
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR
 JP 2007521277 T 20070802 JP 2006-517643 20040625
 US 2006148865 A1 20060706 US 2005-560500 20051212
 PRIORITY APPLN. INFO.: US 2003-483002P P 20030627
 WO 2004-US20353 W 20040625

OTHER SOURCE(S): CASREACT 142:114047
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

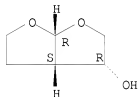
AB The invention relates to a preparation of furofuranyl derivative I, useful as inhibitor of HIV aspartyl protease (no biol. data). For instance, I was prepared via deprotection of II and coupling with III with a yield of 90% (example 2).

IT 156928-09-5P 192725-55-6P
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of furofuranyl derivative useful as inhibitor of HIV aspartyl protease)

RN 156928-09-5 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

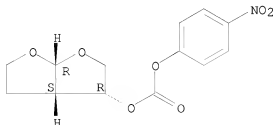
Absolute stereochemistry. Rotation (-).



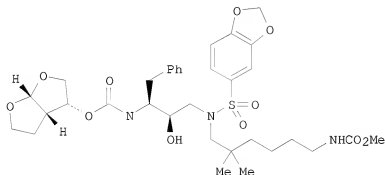
RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L18 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:99287 HCAPLUS
 DOCUMENT NUMBER: 140:339141
 TITLE: Novel arylsulfonamides possessing sub-picomolar HIV protease activities and potent anti-HIV activity against wild-type and drug-resistant viral strains
 AUTHOR(S): Miller, John F.; Furfine, Eric S.; Hanlon, Mary H.; Hazen, Richard J.; Ray, John A.; Robinson, Laurence; Samano, Vicente; Spaltenstein, Andrew
 CORPORATE SOURCE: GlaxoSmithKline, Research Triangle Park, NC, 27709, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(4), 959-963
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 140:339141
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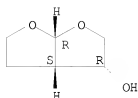


I

AB Furanofuryl analogs of the HIV protease inhibitor amprenavir such as I are prepared in which a terminally substituted n-alkyl group is appended to the N-iso-Bu group of amprenavir and in which the substituents on the N-arylsulfonyl moiety are varied. Some of the inhibitors such as I are found to have greatly enhanced inhibition of HIV protease; the amprenavir analogs also inhibit the growth of both wild-type and resistant strains of HIV and are more effective against the HIV strains than the currently marketed HIV protease inhibitors amprenavir, indinavir, and nelfinavir. E.g., I inhibits wild-type HIV protease with a K_i value of 0.014 pM, and inhibits wild-type and resistant strains of HIV with IC50 values of between 1.6 nM and 15 nM.

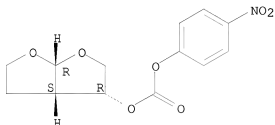
IT 156928-09-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of furanofuryl amprenavir analogs with modifications at the N-arylsulfonyl and N-iso-Bu moieties which show improved HIV protease inhibition and inhibition of wild-type and resistant HIV strains)
 RN 156928-09-5 HCAPLUS
 CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 192/25-55-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation of furanofuryl amprenavir analogs with modifications at the
 N-arylsulfonyl and N-iso-Bu moieties which show improved HIV protease
 inhibition and inhibition of wild-type and resistant HIV strains)
 RN 192/25-55-6 HCAPLUS
 CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl
 ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1999:811207 HCAPLUS
 DOCUMENT NUMBER: 132:49801
 TITLE: Preparation of 1-acylamino-3-(N-arylsulfonyl-N-
 alkoxyamino)-2-hydroxypropanes and related compounds
 as inhibitors of HIV aspartyl protease.
 INVENTOR(S): Sherrill, Ronald George; Hale, Michael R.;
 Spaltenstein, Andrew; Furfine, Eric Steven; Andrews,
 Clarence Webster, III; Lowen, Gregory Thomas
 PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
 SOURCE: PCT Int. Appl., 344 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9965870	A2	19991223	WO 1999-US13744	19990617

WO 9965870 A3 20010315

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2335477 A1 19991223 CA 1999-2335477 19990617

AU 9945760 A 20000105 AU 1999-45760 19990617

AU 767728 B2 20031120

EP 1086076 A1 20010328 EP 1999-928769 19990617

EP 1086076 B1 20041222

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

BR 9912169 A 20010410 BR 1999-12169 19990617

NZ 508855 A 20031031 NZ 1999-508855 19990617

AT 285396 T 20050115 AT 1999-928769 19990617

PT 1086076 T 20050531 PT 1999-928769 19990617

ES 2235492 T3 20050701 ES 1999-928769 19990617

AP 1717 A 20070228 AP 2000-2023 19990617

US 2002049201 A1 20020425 US 2000-731129 20001206

US 6613743 B2 20030902

NO 2000006405 A 20010219 NO 2000-6405 20001215

MX 2000PA12637 A 20010405 MX 2000-PA12637 20001218

HK 1037605 A1 20051007 HK 2001-106764 20010925

US 2004097594 A1 20040520 US 2003-600937 20030620

NZ 528074 A 20041126 NZ 2003-528074 20030908

AU 2004200636 A1 20040311 AU 2004-200636 20040219

US 2006172936 A1 20060803 US 2005-212045 20050825

AU 2007234578 A1 20071213 AU 2007-234578 20071121

PRIORITY APPLN. INFO.: US 1998-90094P P 19980619

WO 1999-US13744 W 19990617

US 2000-731129 A3 20001206

US 2003-600937 B3 20030620

AU 2004-200636 A3 20040219

OTHER SOURCE(S): MARPAT 132:49801

AB ABxN(Gx)CHDCHOR7CH2ND'SO2E [A = H, (substituted) Ht, R1Ht, R1Ak; Ak = alkyl; Ht = cycloalkyl, cycloalkenyl, (substituted) aryl, heterocyclyl; R1 = CO, SO2, COCO, O2C, NR2CO, NR2SO2, etc.; B = null, NR2C(R3)2CO; x = 0, 1; R2 = H, (substituted) Ht, alkyl; R3 = H, (substituted) Ht, alkyl, alkenyl, cycloalkyl, cycloalkenyl; G = null, H, R7, alkyl; G may be bound to R7; D = (substituted) Q, alkyl, alkenyl; Q = (substituted) carbocyclyl, heterocyclyl; D' = OR10, N:R10, N(R10)R1R3; E = Ht, OHT, OR3, NR2R3, (substituted) alkyl, alkenyl, etc.; R7 = H, (CH2O)xY(ZM):(X)Z(M)x, etc.; M = null, H, Li, Na, K, Mg, Ca, Ba, alkyl, alkenyl, etc.; X = O, S; Y = P, S; Z = O, S, N(R2)2, H], were prepared as inhibitors of HIV aspartyl protease (no data). Thus, 3-H2NC6H4SO2NHOCHMe2 (preparation given), tert-Bu N-(1S)-1-[(2S)-oxiran-2-yl]-2-phenylethylcarbamate, and phosphazene base P4 tert-Bu were stirred in 8 h in THF to give 95% tert-Bu N-(1S,2R)-3-[[(3-aminophenyl)sulfonyl] (isopropoxy)amino]-1-benzyl-2-hydroxypropylcarbamate.

IT 192725-55-6 252873-35-1 252873-40-8

252873-50-0 252873-51-1

RL: RCT (Reactant); RACT (Reactant or reagent)

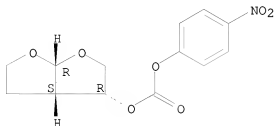
(preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-

hydroxypropanes and related compds. as inhibitors of HIV aspartyl protease)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

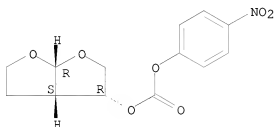
Absolute stereochemistry. Rotation (-).



RN 252873-35-1 HCAPLUS

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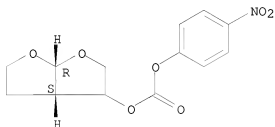
Relative stereochemistry.



RN 252873-40-8 HCAPLUS

CN Carbonic acid, (3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

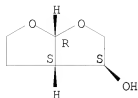
Absolute stereochemistry.



RN 252873-50-0 HCAPLUS

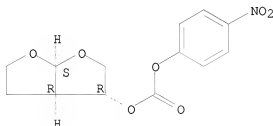
CN Furo[2,3-b]furan-3-ol, hexahydro-, (3S,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



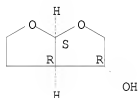
RN 252873-51-1 HCAPLUS
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Absolute stereochemistry.



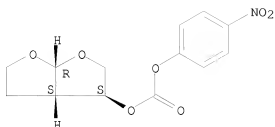
IT 252873-00-0P 252873-01-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of 1-acylamino-3-(N-arylsulfonyl-N-alkoxyamino)-2-hydroxypropanes and related compds. as inhibitors of HIV aspartyl protease)
 RN 252873-00-0 HCAPLUS
 CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aR,6aS)- (CA INDEX NAME)

Absolute stereochemistry.



RN 252873-01-1 HCAPLUS
 CN Carbonic acid, (3S,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:393986 HCAPLUS

DOCUMENT NUMBER: 131:59143

TITLE: Preparation of peptide analogs as retroviral protease inhibitors

INVENTOR(S): Sham, Hing Leung; Norbeck, Daniel W.; Chen, Xiaoqi; Betebeuner, David A.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 572,226, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

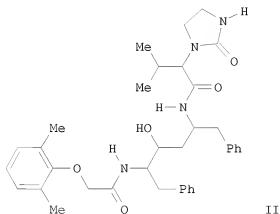
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5914332	A	19990622	US 1996-753201	19961121
CA 2238978	A1	19970619	CA 1996-2238978	19961206
CA 2238978	C	20010515		
CA 2285119	A1	19970619	CA 1996-2285119	19961206
CA 2285119	C	20050920		
CA 2509505	A1	19970619	CA 1996-2509505	19961206
WO 9721685	A1	19970619	WO 1996-US20440	19961206
W: AU, CA, CN, CZ, HU, IL, JP, KR, MX, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9713422	A	19970703	AU 1997-13422	19961206
AU 725369	B2	20001012		
EP 882024	A1	19981209	EP 1996-944941	19961206
EP 882024	B1	20020206		
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CN 1208405	A	19990217	CN 1996-199904	19961206
HU 9901079	A2	19990928	HU 1999-1079	19961206
HU 223782	B1	20050128		
JP 2000502085	T	20000222	JP 1997-522278	19961206
JP 3170292	B2	20010528		
HU 20003305	A3	20001228	HU 2000-3305	19961206
HU 222731	B1	20030929		
JP 2001058979	A	20010306	JP 2000-190510	19961206
EP 1170289	A2	20020109	EP 2001-124290	19961206
EP 1170289	A3	20021113		
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AT 212986	T	20020215	AT 1996-944941	19961206

PT 882024	T	20020731	PT 1996-944941	19961206
ES 2173341	T3	20021016	ES 1996-944941	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
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NZ 510329	A	20040227	NZ 1996-510329	19961206
CZ 293650	B6	20040616	CZ 2000-2210	19961206
CZ 294246	B6	20041110	CZ 1998-1762	19961206
NZ 510328	A	20050128	NZ 1996-510328	19961206
IL 156237	A	20050517	IL 1996-156237	19961206
NZ 338003	A	20050826	NZ 1996-338003	19961206
CZ 296915	B6	20060712	CZ 2004-762	19961206
ZA 9610475	A	19970731	ZA 1996-10475	19961212
TW 494097	B	20020711	TW 1997-86101654	19970213
TW 259178	B	20060801	TW 2000-89115157	19970213
US 6284767	B1	20010904	US 1998-207873	19981208
HK 1016585	A1	20020809	HK 1999-101462	19990409
US 6313296	B1	20011106	US 2000-511390	20000223
US 2002004503	A1	20020110	US 2001-837280	20010418
US 6472529	B2	20021029		
US 2003100755	A1	20030529	US 2002-280652	20021025
US 7279582	B2	20071009		

PRIORITY APPLN. INFO.:

US 1995-572226	B2	19951213
US 1996-753201	A	19961121
US 1996-754687	A	19961121
CA 1996-2238978	A3	19961206
CA 1996-2285119	A3	19961206
EP 1996-943605	A3	19961206
EP 1996-944941	A3	19961206
IL 1996-124607	A3	19961206
JP 1997-522278	A3	19961206
WO 1996-US20440	W	19961206
US 1998-207873	A3	19981208
US 2001-837280	A3	20010418

OTHER SOURCE(S): MARPAT 131:59143
GI

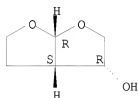
AB R4Z1CONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [I; R1,R2 = lower alkyl,

cycloalkylalkyl, arylalkyl; R3 = lower alkyl, hydroxyalkyl, cycloalkylalkyl; R4 = aryl, heterocyclyl; R5 = N-attached (thi)oxo- or iminoazacycloalkyl; Z1 = Z, O, S, (alkyl)imino, OZ, ZO, NHZ, etc.; Z = alkylene] were prepared. Thus, title compound (S,S,S)-II was prepared in 8 steps from L-phenylalanine. Data for biol. activity of I were given.

IT 156928-09-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)

RN 156928-09-5 HCAPLUS
 CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

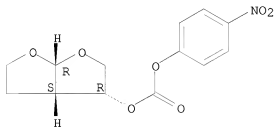
Absolute stereochemistry. Rotation (-).



IT 192725-55-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)

RN 192725-55-6 HCAPLUS
 CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1997:515728 HCAPLUS
 DOCUMENT NUMBER: 127:122001
 TITLE: Preparation of peptide analogs as retroviral protease inhibitors

INVENTOR(S): Sham, Hing Leung; Norbeck, Daniel W.; Chen, Xiaqi; Betebenner, David A.; Kempf, Dale J.; Herrin, Thomas R.; Kumar, Gondi N.; Condon, Stephen L.; Cooper,

Arthur J.; Dickman, Daniel A.; Hannick, Steven M.;
Kolaczowski, Lawrence; Oliver, Patricia A.; Plata,
Daniel J.; Stengel, Peter J.; Stoner, Eric J.; Tien,
Jieh-Heh J.; Liu, Jih-Hua; Patel, Ketan M.

PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 180 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

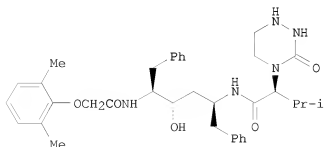
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721685	A1	19970619	WO 1996-US20440	19961206
W: AU, CA, CN, CZ, HU, IL, JP, KR, MX, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5914332	A	19990622	US 1996-753201	19961121
AU 9713422	A	19970703	AU 1997-13422	19961206
AU 725369	B2	20001012		
EP 882024	A1	19981209	EP 1996-944941	19961206
EP 882024	B1	20020206		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
HU 9901079	A2	19990928	HU 1999-1079	19961206
HU 223782	B1	20050128		
JP 2000502085	T	20000222	JP 1997-522278	19961206
JP 3170292	B2	20010528		
HU 20003305	A3	20001228	HU 2000-3305	19961206
HU 222731	B1	20030929		
AT 212986	T	20020215	AT 1996-944941	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
IL 156237	A	20050517	IL 1996-156237	19961206
HK 1016585	A1	20020809	HK 1999-101462	19990409

PRIORITY APPLN. INFO.:

US 1995-572226	A	19951213
US 1996-753201	A	19961121
US 1996-754687	A	19961121
EP 1996-943605	A3	19961206
IL 1996-124607	A3	19961206
WO 1996-US20440	W	19961206

OTHER SOURCE(S): MARPAT 127:122001

GI



I

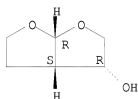
AB R4 -L1-CONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [R1, R2 = lower alkyl, cycloalkylalkyl, arylalkyl; R3 = lower alkyl, hydroxyalkyl, cycloalkylalkyl; R4 = aryl, heterocyclyl; R5 = heterocyclyl e.g. Q - Q4; wherein m, n = 1-3; p = 1,2; X = O, S, NH; Y = CH2, O, S, (un)substituted NH; Z = O, S, NH; L1 = O, S, (un)substituted NH, O-alkylenyl, S(O)m-alkylenyl (wherein m = 0, 1,2), N-(un)substituted NH-alkylenyl, alkylenyl, alkenylenyl, etc.] are prepared Methods and compns. for inhibiting an HIV infection are also disclosed. Thus, (2S)-(4-benzoyloxycarbonylaza-1-tetrahydropyrimid-2-onyl)-3-methylbutanoic acid (preparation given) was condensed with (2S,3S,5S)-2-(2,6-dimethylphenoxyacetyl)amino-3-hydroxy-5-amino-1,6-diphenylhexane using standard coupling procedure [1-ethyl-3-(3-dimethylaminopropyl)carbodiimide/DMF] followed by hydrogenolysis over 10% Pd-C to give the title compound (I). I in vitro at 0.5 nmol inhibited HIV protease by 94.6%.

IT 156928-09-5
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)

RN 156928-09-5 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

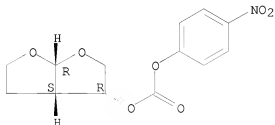


IT 192725-55-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of peptide analogs as retroviral protease inhibitors for inhibiting HIV infection)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

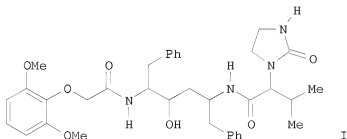
Absolute stereochemistry. Rotation (-).



ACCESSION NUMBER: 1997:515727 HCAPLUS
 DOCUMENT NUMBER: 127:121994
 TITLE: Preparation and formulation of N-(α -aminoacyl)diaminohydroxyalkanes as HIV protease inhibitors
 INVENTOR(S): Sham, Hing Leung; Stewart, Kent D.; Kempf, Dale J.
 PATENT ASSIGNEE(S): Abbott Laboratories, USA
 SOURCE: PCT Int. Appl., 163 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721683	A1	19970619	WO 1996-US19394	19961206
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2238977	A1	19970619	CA 1996-2238977	19961206
EP 876353	A1	19981111	EP 1996-943605	19961206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2000502997	T	20000314	JP 1997-522112	19961206
EP 1295874	A2	20030326	EP 2002-26856	19961206
EP 1295874	A3	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1995-572226	A 19951213
			US 1996-754687	A 19961121
			EP 1996-943605	A3 19961206
			WO 1996-US19394	W 19961206

OTHER SOURCE(S): MARPAT 127:121994
 GI



AB R4ZCONHCHR1CH(OH)CH2CHR2NHCOCHR3R5 [I; R1,R2 = (cyclo)alkyl, aralkyl; R3 = (cyclo)alkyl, hydroxyalkyl; R4 = heterocyclyl or aryl; R5 = N-attached oxoheterocyclyl, etc.] were prepared. Thus, (S)-(PhCH2)2NCH(CH2Ph)COCH2CN (preparation given) was condensed with PhCH2MgCl and the product reduced by NaBH4 to give (S,S,S)-(PhCH2)2NCH(CH2Ph)CH(OH)CH2CH(NH2)CH2Ph. The latter was N-protected and the N-debenzylated product amidated by 2,6-(MeO)C6H3OCH2CO2H (preparation given) to give, after deprotection and amidation by (S)-Me2CHCHR5CO2H (R5 = 2-oxo-1H-imidazol-3-yl) (preparation

given), title compound (S,S,S,S)-II. Data for biol. activity of I were given.

IT 156928-09-5

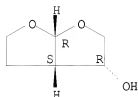
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and formulation of N-(α -aminoacyl)diaminohydroxyalkanes as HIV protease inhibitors)

RN 156928-09-5 HCAPLUS

CN Furo[2,3-b]furan-3-ol, hexahydro-, (3R,3aS,6aR)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT 192725-55-6P

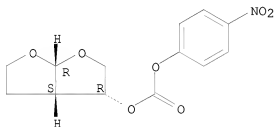
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and formulation of N-(α -aminoacyl)diaminohydroxyalkanes as HIV protease inhibitors)

RN 192725-55-6 HCAPLUS

CN Carbonic acid, (3R,3aS,6aR)-hexahydrofuro[2,3-b]furan-3-yl 4-nitrophenyl ester (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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702.29

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-9.60

-56.80

SESSION WILL BE HELD FOR 120 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 16:14:25 ON 05 FEB 2008